FOOD SAFETY: OVERSIGHT OF THE FDA CENTER FOR VETERINARY MEDICINE

HEARING

BEFORE THE

SUBCOMMITTEE ON HUMAN RESOURCES AND INTERGOVERNMENTAL RELATIONS

OF THE

COMMITTEE ON GOVERNMENT REFORM AND OVERSIGHT HOUSE OF REPRESENTATIVES

ONE HUNDRED FOURTH CONGRESS

SECOND SESSION

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FOOD SAFETY: OVERSIGHT OF THE FDA CENTER FOR VETERINARY MEDICINE

FRIDAY, MAY 10, 1996

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON HUMAN RESOURCES AND
INTERGOVERNMENTAL RELATIONS,
COMMITTEE ON GOVERNMENT REFORM AND OVERSIGHT,
Washington, DC.

The subcommittee met, pursuant to notice, at 10 a.m., in room 2247, Rayburn Office Building, Hon. Christopher Shays (chairman of the subcommittee) presiding.

Present: Representatives Shays, Souder, and Towns.

Staff present: Lawrence J. Halloran, staff director and counsel; Anne Marie Finley and Robert Newman, professional staff members; Thomas M. Costa, clerk; and Cheryl Phelps, minority professional staff member.

Mr. SHAYS. We're going to call this hearing to order. Some of my staff are here for only one reason. And that's to hear me screw up the scientific names that I'm going to have to read.

On March 12 of this year, Food and Drug Administration [FDA] Commissioner Dr. David Kessler told a House Appropriations subcommittee that over a 6-year tenure, "The big nut we have not yet cracked is how we're going to shore up food safety for the future."

Our purpose today is the oversight of the FDA Center for Veterinary Medicine [CVM], which is responsible for two increasingly important aspects of food safety: animal drugs and medicated feeds.

We start with the premise that the American food supply is among the safest in the world. I'm going to repeat that. We start with the premise that the American food supply is among the safest in the world. The question before us today then is whether the CVM, as currently organized and operated, is the tool Dr. Kessler needs to crack the "big nut" of assuring the continued safety of our food.

Food safety for the future depends on the vigilance of regulators and the ingenuity of scientists in detecting and defeating emerging food-borne pathogens. In the past, the known animal diseases had readily visible manifestations and were easily detected by the inspection system still in use today.

But new threats are emerging in far more subtle forms. According to the General Accounting Office, three of the four pathogens considered most important by the Centers for Disease Control, *Campylobacter, Listeria* and *E. coli* 0157, were not even recognized as causes of food-borne illnesses 20 years ago.

These newly recognized microbes and prions challenge the effectiveness and capabilities of the current CVM approach to animal drug reviews and animal feed regulation.

The outbreak of bovine spongiform encephalopathy [BSE], or "mad cow disease," in Britain should send us a stern warning. While no beef or dairy cattle in the United States have been infected with BSE—notice I use BSE this time—our regulatory and public health systems need new tools to fight animal diseases about which there remains significant scientific uncertainty.

There is uncertainty as to the origin and transmission path of the causative agent; and uncertainty, but strong suspicion, about the relationship between BSE, the broader family of transmissible spongiform encephalopathies [TSE's] in animals, and variant forms of Creutzfelt-Jakob disease, which is CJD—I'll use that next—in humans.

Faced with unproven theories as to cause, but undeniable evidence as to effect, the regulatory and industry motto must remain: Better safe than sorry. I guess that's quite an understatement.

It is not enough to say there is no proof of a link between BSE and CJD, when the only available proof can be found in mortality figures. It is not enough to say there is no proof of a direct link between the disease "scrapie" in sheep and BSE in cattle fed on the rendered remains of infected sheep, when no other plausible transmission path explains the spread of these diseases.

Rather than provide a pretext for inaction, the lack of hard proof should compel government and industry to aggressive safety measures that meet every probable, possible, or even theoretical threat. Yes, it may be costly. But the British now know the price of waiting is far higher.

On March 29, 1996, the U.S. Department of Agriculture and the Public Health Service joined the livestock industry in endorsing safety measures to provide additional assurances that the United States remains free of BSE. Included in these steps was a voluntary industry program to stop the use of rendered ruminant animals, sheep, cows, and goats, in feeds for ruminant animals.

Because the BSE, TSE, and scrapie prions are thought to reside in some rendered animal tissues, a ruminant-to-ruminant feeding ban cuts off one possible transmission route of the disease. The FDA pledged expedited consideration of a regulation of ruminant feeds. We will hear more about the agency's plans in that regard today.

We will also hear testimony on the need for new animal drugs, important weapons in the fight to keep animals healthy and stop pathogens before they can be included in food. Continued safety of the food supply requires a drug review and approval process that is accountable and that encourages innovation.

But, as we found with food additive petition reviews, the new animal drug evaluation process can be lengthy and unpredictable. Data provided by the FDA shows that the 1995 review times averaged 20 months, or 600 days. That is far longer than the 180 day period suggested in the statute—not required, but suggested.

Recently, the FDA took steps to improve flaws in the food safety and review process that were the subject of hearings before this

subcommittee in June 1995. We look for similar efforts to improve the CVM drug evaluation program.

While sometimes overlooked in the multiagency U.S. food safety and inspection system, the FDA Center for Veterinary Medicine has a crucial role to perform. As in previous FDA oversight hearings, our task is to examine how well the CVM is performing that role and how well it is prepared to meet emerging challenges with sound science and effective regulation.

I appreciate the contribution of all of our witnesses to our discussion today and I truly look forward to their testimony.

At this time, I'd like to recognize the distinguished gentleman from New York, the ranking member, Mr. Towns.

Mr. TOWNS. Thank you, Mr. Chairman. I'd like to include my entire statement in the record.

Mr. SHAYS. You don't want to read those big words?

Mr. TOWNS. Not at all. Not at all.

I thank you for holding this hearing and, of course, I look forward to hearing from the witnesses. Serious questions have been raised that the FDA may undervalue veterinary science. And as a result, it may be jeopardizing the safety of the human food supply.

These questions seem to stem from budget cuts endured by CVM, apparent delays in CVM's approval of new animal drugs and feeds and FDA policy development on mad cow disease.

I commend you for convening this hearing, Mr. Chairman, not only because I am confident that it will serve to allay unnecessary fears, but because it provides us a forum in which to constructively consider the real problems that forestall the predicted rise in food borne illnesses. For example, I invite our witnesses to share their thinking on H.R. 3200, the Food Amendment and Animal Drug Availability Act of 1996, which I cosponsored with my colleague, Congressman Scott Klug from Wisconsin.

This bill provides the Congress with the legislative tool to reform FDA's operations and procedures as they pertain to the approval of veterinary drugs. I know that FDA and industry have been working closely to revise regulations in this area. As a result of this cooperation, I fully expect that we will have FDA and industry support for legislative reform when the Commerce Committee begins its markup on H.R. 3200.

As I conclude my remarks, I urge all participants in today's hearing to avoid falling victim to the media hysteria surrounding the unfortunate British mad cow disease epidemic. Our review of this matter is not a result of any threat to the U.S. food supply, the public health or deficiencies in FDA regulatory oversight. The FDA represents one of the most personal and dependent relationships American consumers have with their Government. And I say barring none.

We trust the FDA to ensure that our medicine and our medical devices are safe and effective, and that the food we eat every day is free from bacteria, parasites and other harmful substances. Our review of the operation and priorities of the Center for Veterinary Medicine will help lawmakers establish whether this trust is well placed. And, if necessary, make the appropriate corrections.

With these goals in mind, I look forward to working with you, Mr. Chairman, and welcome the views of the FDA and representa-

tives of the food industry, scientific, and public interest communities. This is a very serious issue. And I think it should be dealt with in a very serious manner. But at the same time, we should be directed by facts and not by the news media.

Thank you very much, Mr. Chairman. I yield back.

[The prepared statement of Hon. Edolphus Towns follows:]

OPENING STATEMENT OF THE HONORABLE ED TOWNS SUBCOMMITTEE ON HUMAN RESOURCES AND INTERGOVERNMENTAL RELATIONS

"FOOD SAFETY: OVERSIGHT OF THE FOOD AND DRUG ADMINISTRATION'S CENTER FOR VETERINARY MEDICINE"

MAY 10, 1996

MR. CHAIRMAN, TODAY'S HEARING ON THE FDA'S CENTER FOR VETERINARY MEDICINE PROVIDES US AN IMPORTANT FIRST OPPORTUNITY TO EXAMINE AND REINFORCE THE CENTER'S EFFORTS TO PREVENT ANIMAL-TO-HUMAN TRANSMISSION OF FOOD-BORNE ILLNESSES.

THE U.S. FOOD SUPPLY IS THE SAFEST IN THE WORLD. HOWEVER, ACCORDING TO A GAO REPORT RELEASED TWO DAYS AGO, ESTIMATES OF CASES OF FOOD-BORNE ILLNESSES RANGE FROM 6.5 TO 81 MILLION ANNUALLY, WITH MORE THAN 9000 RESULTING IN DEATH. ANNUAL COSTS DUE TO MEDICAL TREATMENT AND LOST PRODUCTIVITY RANGE FROM 5 TO 22 BILLION DOLLARS.

MORE THAN HALF OF ALL FOOD-BORNE DISEASE AND DEATHS ARE CAUSED BY CONTAMINATED MEAT AND POULTRY PRODUCTS; AND PUBLIC HEALTH AND FOOD SAFETY OFFICIALS BELIEVE THAT RISK OF FOOD-BORNE INFECTION IS ON THE RISE.

CLEARLY, OUR ABILITY TO CONTROL THIS PROBLEM DEPENDS ON THE ABILITY OF CVM TO FACILITATE USE OF DRUGS AND FEEDS THAT INHIBIT DISEASE IN FOOD-PRODUCING ANIMALS.

SERIOUS QUESTIONS HAVE BEEN RAISED THAT THE FDA MAY UNDERVALUE VETERINARY SCIENCE, AND AS A RESULT, MAY BE JEOPARDIZING THE SAFETY OF THE HUMAN FOOD SUPPLY. THESE QUESTIONS SEEM TO STEM FROM BUDGET CUTS ENDURED BY CVM, APPARENT DELAYS IN CVM'S APPROVAL OF NEW ANIMAL DRUGS AND FEEDS, AND FDA POLICY DEVELOPMENT ON MAD COW DISEASE.

I COMMEND YOU FOR CONVENING THIS HEARING, MR. CHAIRMAN. NOT ONLY BECAUSE I AM CONFIDENT THAT IT WILL SERVE TO ALLAY UNNECESSARY FEARS, BUT BECAUSE IT PROVIDES US A FORUM IN WHICH TO CONSTRUCTIVELY CONSIDER THE REAL PROBLEMS AND FORESTALL THE PREDICTED RISE IN FOOD-BORNE ILLNESSES.

FOR EXAMPLE, INVITE OUR WITNESSES TO SHARE THEIR THINKING ON H.R. 3200, "THE FOOD AMENDMENTS AND THE ANIMAL DRUG AVAILABILITY ACT OF 1996", WHICH I CO-SPONSORED WITH MY COLLEAGUE, CONGRESSMAN SCOTT KLUG (R-WI). THIS BILL PROVIDES THE CONGRESS WITH A LEGISLATIVE TOOL TO REFORM FDA OPERATIONS AND PROCEDURES AS THEY

PERTAIN TO THE APPROVAL OF VETERINARY DRUGS. I KNOW THAT FDA AND INDUSTRY HAVE BEEN WORKING CLOSELY TO REVISE REGULATIONS IN THIS AREA. AS A RESULT OF THIS COOPERATION, I FULLY EXPECT THAT WE WILL HAVE FDA AND INDUSTRY'S SUPPORT FOR LEGISLATIVE REFORMS WHEN THE COMMERCE COMMITTEE BEGINS MARKUP ON H.R. 3200.

AS I CONCLUDE MY REMARKS, I URGE ALL PARTICIPANTS IN TODAY'S HEARING TO AVOID FALLING VICTIM TO THE MEDIA HYSTERIA SURROUNDING THE UNFORTUNATE BRITISH "MAD COW DISEASE" EPIDEMIC. OUR REVIEW OF THIS MATTER IS NOT A RESULT OF ANY THREAT TO THE U.S. FOOD SUPPLY, THE PUBLIC HEALTH, OR DEFICIENCIES IN FDA REGULATORY OVERSIGHT.

THE FDA REPRESENTS ONE OF THE MOST PERSONAL AND DEPENDENT RELATIONSHIPS AMERICAN CONSUMERS HAVE WITH THEIR GOVERNMENT. WE TRUST THE FDA TO ENSURE THAT OUR MEDICINES AND MEDICAL DEVICES ARE SAFE AND EFFECTIVE; AND THAT THE FOOD WE EAT EVERY DAY IS FREE FROM BACTERIA, PARASITES, AND OTHER HARMFUL SUBSTANCES.

OUR REVIEW OF THE OPERATIONS AND PRIORITIES OF THE CENTER FOR VETERINARY MEDICINE WILL HELP LAWMAKERS ESTABLISH WHETHER THIS TRUST IS WELL-PLACED, AND IF NECESSARY, MAKE THE APPROPRIATE CORRECTIONS.

Mr. SHAYS. Thank you. I appreciate your helpful words and I agree with them. Also, I am a cosponsor of your legislation and am happy to be. Let me just get some housekeeping things out of the way.

I would ask unanimous consent that all members of the subcommittee be permitted to place any opening statements in the record and that the record remain open for 3 days for that purpose. Without objection, so ordered.

I would also ask unanimous consent that our witnesses be permitted to include their written statements in the record and be able to summarize. Without objection, so ordered.

I would point out before asking and swearing in our two witnesses and welcoming their testimony, we have Dr. Michael Friedman, Deputy Commissioner, Food and Drug Administration. We welcome you to our hearings. Accompanied by Stephen Sundlof, Director, Center for Veterinary Medicine; and Dr. Fred Shank, Director, Center for Food Safety and Applied Nutrition.

You're the first of three panels. We'll have a second panel with veterinarian members from the University of California, Association of American Veterinary Medical Colleges, National Cattlemen's Beef Association, renderers, and we will have a citizen participant. And we will also hear from witnesses regarding animal drugs on our third panel.

So it proves to be a very educational hearing for us. I tell people that being a Member of Congress is like going to school every day and learning new things, and we'll be learning new things. So with that, I would ask our three witnesses to stand up and be sworn in.

[Witnesses sworn.]

Mr. SHAYS. For the record, all three witnesses answered in the affirmative. It truly is our opportunity to have you here today. This hearing is the seventh hearing we've had. You now represent the fourth Center we've had from the FDA and we have two to go. It has truly been very educational. And we appreciate all of you for your service to our country and for the fine work you do. We welcome your testimony, Dr. Friedman.

STATEMENT OF MICHAEL FRIEDMAN, DEPUTY COMMISSIONER, FOOD AND DRUG ADMINISTRATION, ACCOMPANIED BY DR. STEPHEN SUNDLOF, DIRECTOR, CENTER FOR VETERINARY MEDICINE, AND DR. FRED SHANK, DIRECTOR, CENTER FOR FOOD SAFETY AND APPLIED NUTRITION

Dr. FRIEDMAN. Thank you so much, Mr. Chairman. We appreciate this invitation to participate in this hearing, which has been entitled Protecting the U.S. Consumer From Food-Borne Illnesses.

As you've recognized, I'm Michael Friedman. And I'm accompanied today by Dr. Stephen Sundlof, from our Veterinary Center, and Dr. Fred Shank, from our Food Safety and Applied Nutrition Center.

Mr. Chairman, my written testimony deals in more detail with three topics that you've identified specifically as of interest for this hearing. The first is to focus on the performance of FDA's Center for Veterinary Medicine, and we will do so.

The second is to look at the Center's role in the comprehensive effort to protect this country against bovine spongiform

encephalopathy, a disease, which has devastated the cattle industry in England.

The third topic is an update on the Food Additive Petition program of our Center for Food Safety and Applied Nutrition. With your permission, sir, I will take only a few minutes to summarize some of the key points before answering the subcommittee's questions.

It is generally recognized that, except for meat and poultry, which are under the purview of the U.S. Department of Agriculture, FDA has a primary responsibility for the safety of the national food supply. You, of course, recognize the crucial contribution that FDA makes to the safety of meat and poultry through the Center for Veterinary Medicine, which evaluates and approves drugs to prevent, control, and to treat diseases in animals.

It has been estimated that perhaps 80 percent of U.S. livestock and poultry are treated at some time during their lifetime with an animal drug. As a result, the safety and abundance of our meat and poultry are linked to CVM's evaluation and approval of safe and effective animal drugs.

Now, the Center's ability to do this job in turn depends upon two main factors. One is the inherent efficiency of CVM's processes and the other is the availability of resources. Both of these items you all have mentioned in your introductory remarks. With reference to CVM's efficiency, Mr. Chairman, I'm happy to report several encouraging developments, the most important of which is a recent reinvention process of the approval procedures which allow safe and effective new animal drugs onto the market. You have been given written materials in the national performance review format summarizing these changes this morning.

Historically, traditionally, the process consisted of the drug sponsor sending to CVM information regarded as evidence of the drug's safety and effectiveness. And CVM would then respond to the sponsor in a letter. We can elaborate on this in more detail later should you wish. This was an arm's length approach with each party acting wholly on its own and rarely in direct contact with one another.

CVM's new procedures pursue a course which is quite different, and which provides a model that is being explored by other centers within the agency. CVM now encourages the companies to discuss as early as possible their drug projects with the Center's experts, to work closely with them, and afterwards to keep the drug development process absolutely on target. Instead of separation, there is cooperation.

This approach has greatly improved the relationship between CVM and the animal drug industry, and we think has helped speed approval times for their products without compromising any of the standards that are so important for safety and efficacy. It is important to note that CVM takes the statutory time limit extremely seriously and that the vast majority of products in excess of 90 percent of our applications are, in fact, handled in a timely and appropriate manner with action taking place in the prescribed or recommended, as you point out, sir, 180 days or less.

There is a longer period between the first submission and final approval, and we'd like to spend time discussing that later.

There simply are not a substantial number of applications which exceed that deadline. Moreover, the agency continues its consistent commitment to promote better CVM scientific programs. We believe that these are at the heart of CVM's functioning. And our efforts are to at least preserve the Center's resources.

Mr. Chairman, turning to the vexing issue of bovine spongiform encephalopathy or BSE, FDA has been working very closely in the scientific sphere, in regulatory and public health spheres with a number of other crucial agencies and bodies. And we have been carefully considering the probable link between the disease and rendered ruminant products in cattle feed since BSE was first described in the United Kingdom in 1986.

Although no cases of BSE disease have been diagnosed in cattle herds in this country, our industry has, as you pointed out, imposed a voluntary ban on the use of certain products from adult sheep and goats and feed for cattle. FDA subsequently has strengthened the measure by proposing to classify such is not generally recognized as safe, and therefore, subject to FDA approval.

Let me reiterate, just as you did. There is no evidence that BSE has affected any meat producing animal in this country. However, because of the recent British reports of potential association between BSE and an unusual variant form of the human disease, Creutzfelt-Jakob disease, we have put on display today an advance notice of a proposal to raise the level of protection still higher. We propose to ban the feeding of ruminant-to-ruminants of all protein derived from cattle, sheep, and goats. Simultaneously, we are also soliciting public comments and scientific and economic data relevant to other aspects of BSE prevention, including details of rendering or processing practices that could conceivably inactivate transmissible disease.

Finally, I would like to close by briefly describing our response to your request made at the hearings of this committee last June for proposals to improve and define achievable timeframes for the review of food additive petitions. Following that hearing, FDA reviewed its food additive program and has identified several reforms to achieve more predictable and significantly faster petition reviews.

We have also taken substantial steps to reduce the inventory of pending petitions. We expect to bring the total of petitions pending from last June down by 100 by the end of this fiscal year, this fall. And we have set an ambitious goal for achieving timeliness on all of the petitions.

However, because of the increasing complexity of some of the food additive petitions and because of the competition for agency resources, we're also suggesting statutory changes that distinguish between food contact material petitions and the more complicated direct food additive petitions. And set new maximum approval times for each category, which we, as you, take very seriously.

Our proposal is to set a 6-month statutory timeframe extendable to 1 year for complete review of food contact material petitions and a 12-month timeframe which could also be extended for an additional 12 months for complete review of direct food additive petitions. This proposal obviously is predicated upon reasonable flexibility and the ability to reallocate existing resources within the

agency or to develop new external resources. And if approved, the suggested progressive deadlines would be phased in to become effective over a 5-year period.

Mr. Chairman, my colleagues and I appreciate this opportunity to address you. We'd like to try and answer any questions you may have. Thank you.

[The prepared statement of Dr. Friedman follows:]

Mr. Chairman,

Thank you for the opportunity to participate in today's hearing on "Protecting the U.S. Consumer from Food Borne Illnesses." My name is Dr. Michael Friedman. I am the Deputy Commissioner for Operations at the Food and Drug Administration (FDA). With me today are Dr. Stephen Sundlof, Director, Center for Veterinary Medicine and Dr. Fred Shank, Director, Center for Food Safety and Applied Nutrition.

As you are aware, the United States food supply is one of the safest, most abundant, and most affordable in the world. This has been accomplished through a program that relies on science, cooperative efforts with government agencies at all levels, increased cooperation with our international counterparts, as well as interaction with academia, industry, and consumers. FDA is committed to ensuring safety, and working to protect the American consumer from unsafe, adulterated, or misbranded food. The agency strives to improve its existing monitoring programs, research, product approval processes, and enforcement efforts. To these ends, we welcome your ongoing interest in this subject.

My discussion of food safety will center on foodborne pathogens in food derived from animals, which you have indicated is the focus of this hearing. I plan to describe what FDA is doing to protect the food supply from these pathogens; the roles of FDA's Center for Veterinary Medicine (CVM) and Center for Food Safety and Applied Nutrition (CFSAN) in developing policies to control foodborne pathogens; and how we work collaboratively with our federal and state counterparts to protect the public health by safeguarding the food supply.

FOOD SAFETY

Virtually all food available to the U.S. public is wholesome and unlikely to cause illness to the consumer. However, as with most things, health risks do exist. Foodborne illness originates from a variety of sources. Pathogenic organisms, such as viruses, bacteria, and parasites, represent the most widely recognized causative agents and are the focus of my remarks as you have requested in your letter of invitation. Other foodborne risks such as naturally occurring toxicants, animal drug residues, pesticides, and environmental contaminants also have the potential, individually or in combination, to be the cause of

illness. Moreover, food production practices, processing, storage, distribution, handling and home preparation techniques either individually or in combination have the potential to increase the risk of microbiological or chemical caused illness. However, risks caused by chemical contaminants and food production practices are not the focus of my remarks for today's hearing.

Foodborne illness is not a new form of disease, nor is it one-dimensional. Foodborne illnesses have been with us as long as man has walked the earth. In the United States, foodborne microbial illness is a major cause of personal distress, preventable death, and avoidable financial loss. Several studies conducted over the past 10 years have indicated that an estimated 6.5 million to 81 million people become ill from pathogens in food every year, resulting in an estimated 9,000 deaths.

It is worth noting that the majority of the illnesses that occur are mild and of short duration and frequently are not even diagnosed. However, a small fraction can produce immediate, acute effects, sometimes involving many people in a single episode, with reactions ranging from gastrointestinal upset to

death. There is also the potential for chronic, or long term risks, but these are not as clearly quantifiable.

Examples of some foodborne pathogens originating in animals include *Salmonella spp.*, i.e., *Salmonella enteritidis*, *Campylobacter jejuni*, and *Escherichia coli* O157:H7.

Salmonella spp. are bacteria that cause gastrointestinal disease (nausea, vomiting, abdominal pain, diarrhea, fever, and headache), that is sometimes fatal. The illness has been associated with consumption of many different foods, including raw meats, poultry, eggs, milk and dairy products, fish, shrimp, frog legs, yeast, coconut, sauces and salad dressings, cake mixes, cream-filled desserts and topping, dried gelatin, peanut butter, cocoa, chocolate, and melons. The infectious dose may be very small. Infections with *Salmonella* may be followed by chronic arthritis symptoms three to four weeks after onset of acute symptoms. *Salmonella enteritidis* bacteria cause gastrointestinal disease (abdominal pain, nausea, diarrhea, vomiting, and fever) which has often been associated with consumption of undercooked or raw eggs. As with other *Salmonella spp.*, the infectious dose may be very small, and infection may be

followed by enteric fever, septicemia, or chronic arthritis symptoms.

Campylobacter jejuni bacteria cause campylobacteriosis, a gastroenteritis (watery diarrhea, malaise, fever, abdominal pain) associated with consumption of foods of animal origin, especially poultry and raw milk. A chronic symptom which may follow infection includes Guillain-Barré syndrome.

Escherichia coli O157:H7 is a verotoxin-forming bacterium that causes hemorrhagic colitis and may, in the very young and the elderly, cause the sometimes fatal hemolytic uremic syndrome. Hemolytic uremic syndrome is characterized by renal failure. The infectious dose may be very low. Undercooked or raw ground beef, salami, mayonnaise-based salad dressings, raw milk, yogurt, and apple cider have been implicated in outbreaks and sporadic cases.

As you can see from the list above, the most likely animal-derived foods which present risks of food-borne disease are meat, poultry, milk, seafood and eggs. Food derived from animals can

be exposed to these pathogens on the farm, at slaughter, or through mishandling anywhere from the farm to the table.

REGULATING FOOD SAFETY

FDA is responsible for regulating the safety of a great many foods, including eggs, seafood, and dairy products. The U.S. Department of Agriculture (USDA) has the primary authority for regulating meat and poultry. FDA also is responsible for the safety of animal feeds. A significant part of FDA's responsibility is to keep both human foods and animal feeds free of microorganisms such as fungi or bacteria, and their toxins (mycotoxins and bacterial toxins), illegal residues of drugs, pesticides, and environmental contaminants that are harmful to public health. Our agency carries out these responsibilities in cooperation or partnership with other federal or state organizations by: working with the animal health industry to ensure that safe and effective drugs are available to treat animal diseases, particularly those that may impact human health; conducting and facilitating research in the area of food safety; inspecting firms; sampling and analyzing products to determine if the producers of these goods have complied with the provisions of

the FDC Act; taking appropriate enforcement actions when the agency finds that firms are not complying with the law; and providing guidance, training, and technical assistance. But, the law places the burden of ensuring that animal drugs are used safely and appropriately and that contaminants are controlled as much as possible in the production of food through observance of good manufacturing practice (GMP), on food manufacturers, producers, and distributors.

FDA's food safety programs have evolved over many years to become both broad reaching and highly specialized. This evolution occurred due to a number of factors that, together, make the regulation of food an unusually complex undertaking.

Our program has three fundamental safety objectives: (1) targeting our efforts toward controlling known "acute" type pathogens (e.g., salmonella), through the use of safe and effective animal drugs and feed additives to treat infected animals, and other prevention programs; (2) monitoring the food supply in coordination with other agencies in order to prevent the consumption of unsafe food and to gather information on the known or emerging pathogens (i.e. transmissible spongiform

encephalopathies); and (3) learning more about potential long term problems and taking steps to lower long term risk.

I would now like to describe some things that we are doing to meet these objectives with regard to foodborne pathogens.

CENTER FOR VETERINARY MEDICINE (CVM)

Prevention of human illness from foodborne pathogens may begin with control of the pathogen in its animal host. CVM is responsible for evaluating and approving drugs to prevent, control, and treat diseases in animals. This includes food-producing animals, as well as companion pets and exotic animals. FDA requires drug sponsors to show that each new animal drug, including those intended for use in animal feeds, is safe and effective for its intended use before it can be approved for marketing. When a drug is used in food producing animals, CVM's charge is to assure that any food derived from the animals (meat, eggs, seafood, or dairy products) is free from potentially harmful drug residues. Evidence substantiating safety and effectiveness in the target animals, and safety of any food

derived from treated animals must be submitted by the drug sponsor to CVM for evaluation by its scientific review experts.

Once a drug is approved, CVM monitors the drug's continued safety and effectiveness through post-marketing surveillance programs. An estimated 80 percent of U.S. livestock and poultry are treated with an animal drug during their lifetime. The availability of safe and effective drugs for use in food-producing animals has benefited the consuming public by increasing production at reduced cost, and improving the quality of these food items, while ensuring the safety of these foods.

The challenges faced by CVM in the area of food safety have become more complex over the last several years as the technology of food production has advanced. Animals are now grown in high density production facilities which have increased the efficiency of food production, but which also have put additional stress on the animals and made the control of diseases critical. Furthermore, recent changes in drug manufacturing production technology have created new and more sophisticated types of animal drugs for CVM to evaluate. Each of these advances presents a unique situation that must be evaluated before the

drug can be approved. And, because of the newness of the technology associated with some of these drugs, the CVM has also had to respond to concerns about the public's perceived threat from the use of these new technologies. Such was the case in recombinant Bovine Somatotropin.

Aside from new safety issues in food production, technological advancements in recent years have also had a significant effect on the number of requests by drug sponsors to CVM for review. During the last six fiscal years, CVM has experienced a 29% increase in the number of submissions for review (from 5880 in 1990 to over 7595 in 1995). At the same time, the CVM's resources have decreased in terms of budget and manpower. In the face of increasing workloads and decreasing resources we have searched for innovative ways to lessen the impact of these trends.

Reinventing the New Animal Drug Approval Process

Recently, CVM has undertaken a major initiative to reengineer the review and approval process for new animal drug applications (NADAs). This initiative has already proven to be a more speedy and effective process, which will serve to make more animal drugs available to treat animal disease.

The traditional animal drug approval process was very segmented. The drug sponsor decided what information would prove that a drug was safe and effective, and then the information was collected, compiled and submitted to the CVM for review. The CVM evaluated all the data and informed the sponsor of its assessment. If there were any deficiencies, the firm would collect more data, compile and submit it, and wait for CVM's decision. This process resulted in numerous iterations before the drug was finally approved. It was also very resource and time intensive.

Our new approach focuses on encouraging sponsors to involve CVM in their drug development process as early as possible, and encourages an interactive approach throughout the planning, research, and review of the drug. In this way, CVM and the drug

sponsor can agree on requirements for the approval of a drug used for the specific indication, and identify any data needed. This approach helps the sponsor reach an understanding with CVM before development is started so that any project undertaken has an increased probability of resulting in the approval of the product. It also allows for modifications to the drug development plan to address any unexpected results as information becomes available.

The response from the participating sponsors has been very positive. They believe this new approach has proven itself to be beneficial in increasing the efficiency of the drug approval process. It also benefits them by assisting in management and coordination of their limited resources during drug development.

Some specific initiatives that are part of this reengineered drug approval process are:

Pre-Submission Conferences - CVM is encouraging sponsors of new animal drugs to participate in pre-submission conferences where the sponsor's objectives and CVM's requirements are discussed in detail. The result of these conferences is agreement on the

information necessary to support approval for the desired use of the drug. These conferences help the sponsors to focus their efforts toward conducting studies which are pivotal in determining whether the drug is safe and effective, and help to decrease complaints about unexpected new requirements.

Review of Study Protocols - Although not required by regulation or statute, CVM is strongly encouraging sponsors to submit protocols for any pivotal studies for CVM's input and concurrence. Using this procedure to assure that the design of a study will result in adequate information to evaluate the drug, any subsequent shift in review personnel is seamless to the process. Although resource intensive to FDA, CVM believes this initiative will ultimately save time and make the drug approval process much more efficient, and has committed itself to a 50 day review time for protocols. The review of protocols enable reviewers to evaluate studies in a more timely manner, and the sponsors to embark on a development plan with more comfortable understanding and agreement with FDA on the requirements.

Phased Review of Data Submissions - Instead of waiting until all the supporting information is collected and compiled, the

sponsors are now encouraged to submit critical studies during their drug development in the form of an Investigational New Animal Drug Application (INADA). CVM will then review the results of these studies so that any new concerns can be addressed prior to submitting a full NADA. It is advantageous to both the drug sponsor and CVM in identifying unexpected problems in the research, and facilitating any necessary modifications to the drug development. For example, early review of a dose determination study will ensure that clinical trials for efficacy and target animal safety are conducted with the effective formulation and dose of the drug.

Direct Review of Submissions - Another innovation to increase the efficiency of the review process is the distribution of administrative processing responsibilities to those areas responsible for the scientific evaluation of the data submitted for review. Previously, CVM endorsed the concept of a project manager for each drug product. This added a point of quality control with one CVM employee responsible for the drug product and its current status, but it was extremely resource intensive. This direct review process, linked with the phased review policy, has encouraged a more interactive and efficient review process.

This distribution is only possible because the Center has a tracking system that can be used as a "Virtual Project Manager" that monitors the current status of the drug development. Although the tracking system and this policy is relatively new, both the sponsors and the scientific review staff believe this level of interaction has benefited the drug approval process tremendously.

Sponsor-Monitored Methods Trials - We have shifted the primary responsibility for validation of regulatory methods to the sponsor. Instead of relying on government laboratories (with other competing priorities) to schedule and complete a method trial, the sponsor may now contract with non-government laboratories to conduct method trials. This ensures prompt conduct of the necessary trials, and although both USDA and FDA laboratories may still participate in the method trial, this change assures that there is an adequate number of laboratories available for timely completion of this phase of drug approval.

CVM has implemented several other initiatives to improve drug availability, reduce regulations, increase food safety, and

support the reengineered drug approval process. These initiatives include:

Expedited Review Status for New Animal Drugs - New and innovative products, such as a new chemical entity not yet approved for use in animals, or a drug targeted for a disease condition that has no approved therapy are important advances that may significantly impact on food safety. If a drug qualifies for CVM's expedited review program, target times for review of data are reduced from the statutory 180 days to 90 days. Since 1982, the center has granted expedited review status to 32 documents (3 NADAs, 1 Public Master File, and 28 INADAs for expedited data review).

Updated Guidance Documents - CVM has also focused on updating several guidance documents. These serve as aids to industry for various portions of drug development. Over the last several years, documents have been finalized to provide guidance for development of study protocols, clarification of responsibilities of clinical investigators, evaluation of food additives for fish, and submission of manufacturing chemistry master files. Several other documents are in various stages of preparation or revision,

including efficacy and/or animal safety requirements for carcass quality, anticoccidial, anthelmentic and mastitis drugs.

Data Integrity - Improvements in the regulated industry's data collection and quality assurance is increasing the efficiency of the data review process within the CVM. This has been accomplished through use of guidance documents, workshops, and other educational initiatives. With the drug sponsors assuming more responsibility for the type and quality of data submitted for review, we can focus our resources on the evaluation of the studies with regard to the effect of the drug.

Treatment INADs for Minor Species - Approval of drugs for minor animal species (i.e., many pets, aquaculture species, exotic animals) provide limited incentive for traditional pharmaceutical sponsor drug development, and these voids in availability of therapy can impact on food safety. CVM has developed a system of "treatment INAD's" and "public master files" that allow clinical data to be gathered by those that need the drugs. The collected data are placed in public master files for future reference by pharmaceutical sponsors in support of NADAs. Public funds from USDA's National Research Supported Project No. 7 (NRSP-7) are

also directed to this effort. NRSP-7 is a federally funded program established to assist animal producers and veterinarians obtain FDA approval of drugs for minor uses.

Environmental Requirement Changes - Based upon ten years of reviewing environmental assessments for animal drugs, CVM has found that many of the applications and requests that currently require assessments have no significant impact on the environment. Therefore, the agency is proposing to exclude these uses from preparing an environmental assessment. In most cases, elimination of these environmental assessments will result in no additional risk to the environment and will provide a substantial savings to the regulated industry and CVM. However, we will be coordinating this policy with EPA in case there are situations that do not have the potential for environmental impact. This focuses the agency's environmental review resources on those areas that have potential for significant environmental impacts.

STARS - CVM implemented a new Submission Tracking and Reporting System (STARS) in November 1992. This database plays a critical function in monitoring the status of CVM's pending applications and files. It assists in coordinating scientific reviews and

CVM's responses to the industry's requests. With this new system, prioritized time frames are assigned to submissions based on the type of request and the amount and complexity of the data the firm submits. STARS has helped CVM focus to assure a complete and coordinated response to sponsors' applications. This database has also enabled the implementation of phased review and direct review of drugs, by providing a tool to help manage the complex process associated with drug approval.

CVM's Food Safety Programs

CVM has initiated several programs and research projects that are designed to help prevent harmful pathogens from being transmitted to humans through the food supply and/or the environment. These include CVM's:

Bacterial Susceptibility Monitoring Program - CVM has initiated a collaborative bacterial susceptibility monitoring program with other FDA Centers, USDA, and the Center for Disease Control and Prevention (CDC), in response to the recommendations of an FDA Advisory Committee on fluoroquinolone antibiotics and a 1995 American Society of Microbiology Task Force on Antibiotic

Resistance. This program grew out of concerns by FDA and other scientific experts about how to best maintain antibiotic effectiveness, ensure safety, and increase the availability of new products to veterinary practitioners and the food animal industry. Because the development of bacterial resistance to existing drugs or to future approved products would negatively impact both efficacy and safety, FDA has made the susceptibility monitoring a priority program.

The national surveillance program will monitor changes in bacterial susceptibilities of zoonotic pathogens from human and animal clinical specimens, from healthy farm animals, and from carcasses of food-producing animals at slaughter plants. Prior to this program, there was no comprehensive national or global surveillance system for monitoring antimicrobial resistance of enteric pathogens in humans or animals and none at all which combined the two populations.

Through this new program, baseline susceptibility patterns of *Salmonella* isolates from animals and *Salmonella* and *E. coli O157:H7* isolates from humans already have been determined. The susceptibility profiles of these isolates form a baseline to

which future changes in susceptibility and emergence of new resistance can be compared. On-going monitoring is underway at USDA's Agricultural Research Service's National Animal Disease Center in Ames, Iowa and at CDC's Foodborne Disease Laboratory in Atlanta.

The problem of antimicrobial resistance is complex and requires collaborative efforts by several agencies; the establishment of FDA's monitoring program is a significant milestone to its solution.

Salmonella Control Program in Feed and Feed Ingredients - In September 1990, CVM announced a program for attaining *Salmonella* negative feed ingredients and finished feeds. Since then, CVM has held numerous meetings with representatives of industry, academia, and other Federal and State agencies to coordinate the work of achieving *Salmonella* negative feed.

CVM initiated the formation of a Federal-State Steering Committee in July 1991. The Committee requested that the United States Animal Health Association (USAHA) serve as a scientific forum for debate on the means to best eliminate harmful microbial

contamination from feed. In October 1991, USAHA established the Feed Safety Committee to serve as a venue for the forum. The work of this committee was divided among four subcommittees. The subcommittees are live production (poultry, beef, pork, dairy, and aquaculture); microbiology (sampling and techniques); feed manufacturing (to include ingredients, equipment, and additives); and feed transportation. The membership of the Feed Safety Committee and the Subcommittees consists of members of government industry and academia.

We believe that the best way to reduce Salmonella contamination in feed is through a quality assurance program and to achieve this we are focusing on the Hazard Analysis Critical Control Points (HACCP) approach. The *Salmonella* contamination which occurs during the production, and during storage and transportation, is largely preventable. Major segments of the feed industry have developed HACCP plans. To further reduce *Salmonella* contamination of feed requires that each manufacturer tailor a HACCP plan to each feed manufacturing facility. Currently, several firms in the feed and feed ingredients industries are working on developing generic HACCP plans. CVM encourages the feed industry to actively seek industry wide

acceptance of HACCP-based plans. CVM is prepared to offer comments on specific plans if requested.

CVM also has reveiwed five Food Additive Petitions (FAP) for chemicals or processes to control Salmonella in feed have been accepted for review. Two have been approved, one is under review, and two are inactive because of the lack of adequate information from the sponsor.

On September 28, 1995, the regulations were amended to permit the irradiation of complete poultry feeds and poultry feed ingredients to achieve *Salmonella* negative feed. Based on the scientific information, we believe that this irradiation will also be effective against *E. coli*.

On April 9, 1996, the regulations were amended to permit the use of formaldehyde as an antimicrobial food additive for maintaining poultry feeds *Salmonella* negative for up to 14 days. Again, while the specific approval is for *Salmonella* control, the scientific literature suggests that the formaldehyde will also be effective against other common microbes in feed.

The approval of FAPs with antimicrobial activity is an important step toward the goal of *Salmonella* negative feed and of improving the safety of feed for animals and ultimately, increasing the safety of food products of animal origin.

Research - Research in CVM has as its mission the application of current scientific procedures to the solution of CVM regulatory issues. The primary focus of CVM's research is food safety. While CVM's food safety responsibilities encompass foodborne diseases, its resources address this particular aspect of human health primarily through the need to ensure that safe and effective animal drugs are available to treat these diseases.

Particular importance is placed on the priority for research in CVM. Recent Congressional interest in CVM has focused on the potential for drug residues in animal derived food and the availability of residue detection methods for monitoring. Drug residues in milk have been of particular interest to Congress and the subject of GAO reports.

The food safety focus of CVM research also has included the development and evaluation of procedures necessary to detect

unsafe residues of unapproved animal drugs, metabolism studies in domestic animals as well as fish, evaluation and approval of drug residue screening tests for milk, and current issues on zoonotic disease of importance in domestic animals. All these programs are directed to food safety by ensuring that there are no unsafe drug residues in animal derived food; and by minimizing the human risk from animal disease by ensuring the health of domestic animals. Through a Federal/State/industry cooperative program, involving the National Conference on Interstate Milk Shipments and the milk industry, all Grade A milk is now screened with evaluated screening tests for beta-lactam drugs prior to introduction into the food chain.

Under the umbrella of food safety, CVM has supported studies on zoonotic disease in animals which could be transferred to humans. Animal feeds are considered a source of *Salmonella spp.* in animals and therefore, a source of this disease in humans. CVM research has been directed to the evaluation of procedures to detect *Salmonella spp.* in feeds.

CVM has previously conducted studies on the human health issue of the transfer of resistance organisms from animals to humans.

Earlier studies were designed to develop data on comparison of *Salmonella spp* and *Campylobacter jejuni* in foods of animal origin and the occurrence of human illness caused by those two organisms. Other CVM research on the area of zoonotic disease has been to quantify the extent of drug resistance in select pathogenic bacteria isolated from food-producing animals. These studies were a primary reason for the current regulation requiring the development of data for new antibiotics on the shedding of resistant organisms from the use of the antibiotic in food producing animals.

Animal Drug Availability Legislation

FDA also recognizes that statutory changes also may be appropriate to make more animal drugs available to treat sick animals. FDA has worked very closely with the animal health industry to develop language that will provide adequate flexibility in the approval process while maintaining public and animal health safeguards. Although the agency still has several significant concerns with language proposed in bills before Congress, the agency has been actively involved in discussions with the animal health industry coalition to address our

concerns. Our discussions have also included the possibility of an important new category of animal drugs for use in feed, "Veterinary Feed Directive Drugs." We are encouraged by the way these discussions are moving and hope that they may result in a bill that both the industry and Agency can support.

MONITORING THE FOOD SUPLY

In the United States, the protection of the public from unsafe microbes in food is a shared responsibility between FDA, CDC, and USDA at the federal level, and state and local government agencies at their respective levels. CFSAN and FDA's Office of Regulatory Affairs (ORA) have the primary responsibility in this area for the Agency.

CDC Surveillance Program

Effective surveillance is key to tracking foodborne pathogens. Such surveillance provides policy makers and health professionals with the basis for developing, implementing, and evaluating control policies that will lead to a healthier United States population in the new millennium.

Science is providing the regulatory community with new information, often through the use of sophisticated genetic techniques, which help us identify weaknesses in our system and points where preventive intervention strategies may be applied. From current epidemiologic data, we can conclude that our most important foodborne hazards are microbial, primarily *Salmonella* spp., *Campylobacter jejuni*, and *Escherichia coli (E. coli)* O157:H7. The Public Health Service has included foodborne disease risk reduction in the national health promotion and disease prevention objectives of Healthy People 2000. These objectives include reductions in the numbers of foodborne infections with *Salmonella spp.*, *Campylobacter jejuni*, and *E. coli* O157:H7, and reductions in the number of outbreaks of *Salmonella enteritidis* infections.

CDC's experience with newly emerging foodborne pathogens, well-recognized pathogens appearing in new foods, and foodborne illnesses in immunocompromised consumers, suggests that foodborne disease is an ever changing public health challenge--a problem of emerging infectious disease. In partnership with representatives from state health departments, other federal agencies, medical and public health professional associations, and international

organizations, CDC has developed a strategic plan entitled "Addressing Emerging Infectious Disease Threats: A Prevention Strategy for the United States."

To assure close coordination and adequate support for this program, CFSAN has assigned one of its employees to CDC as a full-time liaison. FDA and USDA have also transferred funds to CDC to help support this program.

FDA's Role in Monitoring the Food Supply

One important aspect of FDA's food safety program is its inspectional strategy. Inspections can determine the adequacy of conditions in a food plant at the time of the inspection, but not whether the company is operating reliably and consistently, over the long term, to produce safe food. Furthermore, the current system of regulatory controls is reactive, not preventive. That is, the system generally relies on detecting and correcting problems after they occur, rather than preventing them in the first place. Only in certain limited areas, such as low-acid canned foods, are mandated preventive controls currently in place.

FDA believes that it is time to consider improvements in the system and adopt a Hazard Analysis Critical Control Point (HACCP) approach to food safety, particularly for seafood. Such a change has been endorsed by such authoritative organizations as the National Academy of Sciences (NAS), the Codex Alimentarius Commission and the National Advisory Committee on the Microbiological Criteria for Foods (NACMCF).

As described by the NACMCF, HACCP has seven basic steps. It begins with an in depth analysis of potential hazards, followed by identification of points in the processing operation (critical control points) where the failure to control the hazard is likely to result in illness or injury to the consumer. Steps three and four are the establishment of critical limits associated with each identified critical control point and delineation of procedures to monitor the limits. The firm identifies corrective action procedures to be taken when monitoring indicates that a critical limit has been exceeded. Then, an effective recordkeeping system must be in place to document the HACCP system. Finally, the HACCP system should be verified to assure that it is functioning properly.

Actually, HACCP is not new. The FDA's low acid canned food program, established in 1973, uses HACCP principles. This program has been very effective in assuring the safety of canned foods.

In December of 1995, FDA issued a final rule for mandatory HACCP for the seafood industry, to become effective on December 18, 1997. Because we believe the future of food safety lies with the HACCP approach, FDA announced, in an August 1994 advance notice of proposed rulemaking, that it is considering the development of HACCP regulations for other segments of the U.S. food supply, including domestic and imported foods. FDA also initiated a program to help the agency obtain additional information and experience on whether, and how, to design HACCP systems for foods other than seafood. Seven major food companies are participating in FDA's HACCP pilot program, and the products involved represent a wide range of foods, manufacturing processes, and hazards.

HACCP takes on even more importance with globalization of the food supply and the need for a consistent system for assuring trading partners of the safety of imported products. The U.S. is importing more food, often in processed form rather than raw,

than ever before. In the early 1970's, all imported products regulated by FDA numbered approximately 500,000 formal entries (i.e., those valued at $1250 or more). In 1995, 1,300,000 food products alone entered the U.S. Likewise, U.S. exports are increasing yearly. The U.S. must be prepared to demonstrate that American products introduced into international commerce meet high standards of quality and safety. Industry use of HACCP procedures is one way of accomplishing this. In fact, the European Union has incorporated the HACCP system into food safety standards and directives.

FDA's model *Food Code* also incorporated a framework for the application of HACCP at retail. The Food Code provides a set of food handling recommendations that can be used as models for retail establishments such as restaurants, grocery stores, vending operations and nursing homes. Its primary focus is the prevention of foodborne illness. The Food Code includes input from many sources, including the Conference for Food Protection, Association for Food and Drug Officials, industry, other federal agencies and academia.

Cooperation with Other Organizations

One of the most important and cost-effective ways in which FDA works to assure the safety of the nation's food supply is through cooperative efforts with other federal, state, and private organizations. While FDA has traditionally collaborated with USDA and CDC, the intensity of our cooperation has increased significantly in the last several years. FDA and USDA have placed full-time liaisons at CDC to ensure that all foodborne illness activities are fully coordinated.

The federal agencies have also increased collaboration and cooperation with state and local agencies that have primary responsibility for regulating the activities of the retail segment of the food industry. We also have increased collaboration with trade associations, such as the National Food Processors Association and the Grocery Manufacturer's Association, to gain their support and cooperation in implementing food safety programs, and with training organizations, such as the Food Marketing Institute and the Educational Foundation of the National Restaurant Association,

which conduct training programs and disseminate information on food safety to their members.

The agencies participate in numerous forums to discuss foodborne disease. These forums include:

Healthy People 2000: National Health Promotion and Disease Prevention Objectives, a prevention initiative to improve the health of the American people during the decade of the 1990s. One of the 22 priority areas is food and drug safety. FDA is the lead agency for this priority area, working closely with CDC and USDA and through the states and non-government organizations. Healthy People 2000 tracks yearly progress in food safety improvement through four objectives, including tracking the incidence of five foodborne bacterial diseases.

The National Advisory Committee on Microbiological Criteria for Foods (NACMCF), an advisory committee formed in 1987 by USDA and coordinated by FSIS, FDA, National Marine Fisheries Service, and the Department of Defense. The Committee provides impartial scientific advice to federal food regulatory agencies for use in the development of an integrated food safety system approach to

ensure the safety of domestic, imported, and exported foods. NACMCF has provided the agencies with outstanding advice, including development of HACCP principles, which are now incorporated in the HACCP programs mentioned above.

The Conference for Food Protection, comprises representatives from regulatory agencies at all levels of government, the food industry, academia, and consumer organizations. Its goal is to promote food safety at retail by identifying and addressing problems, providing uniform procedures, and promoting mutual respect and trust by establishing a working liaison among all parties concerned with food safety.

The Food Safety and Nutrition Education Task Force, co-chaired by FDA and an industry trade group, comprises food and nutrition consumer affairs and education representatives from industry, trade, consumer and public health organizations, government agencies, and public affairs firms. This group focuses on education strategies and initiatives.

The National Center for Food Safety and Technology (NCFST), a cooperative government/academia/industry research endeavor that

includes the Illinois Institute of Technology (IIT), the IIT Research Institute, the University of Illinois Food Science Department, FDA/CFSAN, and food-related industries. Cooperative research endeavors at the NCFST provides FDA scientists access to highly technical expertise and provides the opportunity to conduct critical food safety research, which could not have been attained by FDA alone.

The Columbus Center CFSAN seafood and molecular biology researchers will soon be located at the Columbus Center in Baltimore's Inner Harbor. They will focus on applying new technologies to enhance the safety of the food supply for the American consumer. In this state of the art facility, CFSAN scientists will combine their expertise conducting research in molecular biology and seafood safety. Their research will be used to develop and evaluate new scientific approaches which aid the FDA in accomplishing its mission.

The University of Maryland On April 15, 1996, FDA entered into a partnership with the University of Maryland. Under this partnership, internationally recognized scientists from both organizations will share their expertise on significant issues

pertaining to food safety, nutrition, and food science. We believe that pooling resources will enhance our ability to acquire and maintain state-of-the-art science facilities and equipment. Four areas of emphasis include: 1) the development of enhanced methods for detecting foodborne pathogens, contaminants, and toxins; 2) the designing of nutrition and clinical studies to better assess nutrient quality, safety, and proper labeling; 3) the evaluation of technological innovations that will assist in the review of food ingredients, risk assessment, international standards, and educational research; and 4) the ability to better anticipate and respond to technological developments that affect consumers, their behavior and the food industry.

Seafood HACCP Alliance and the Meat and Poultry HACCP Alliance, an affiliation of federal, state, industry, and academic organizations that, working together, have developed curricula to conduct training programs to facilitate the implementation of HACCP. These training programs will formally begin in the summer of 1996.

The *Salmonella enteritidis* Interagency Working Group, an integrated coordinated approach to the control of *S. enteritidis*

in eggs. The group comprised representatives from USDA (FSIS, APHIS, Agriculture Marketing Service, Agriculture Research Service); CDC; FDA (Center for Food Safety and Applied Nutrition); the U.S. Animal Health Association; representatives from the egg industry; state animal health departments; and state departments of public health. The working group has considered issues like quality assurance programs as an alternative to the USDA *S. enteritidis* traceback regulation and requirements for the refrigeration of eggs during transportation and storage.

Implementation Group on Emerging Infectious Diseases, an interagency working group of the Committee on International Science, Engineering and Technology (CISET), formed in December, 1994. It published a report on emerging and re-emerging infectious diseases, including foodborne diseases, in September, 1995. Five sub-working groups, chaired by representatives from CDC, FDA, the National Institutes of Health (NIH), U.S. Agency for International Development, the Department of Defense (DOD) and the State Department, and including outside experts from academia, industry, and non-profit organizations are now working on implementation of recommendations from that report.

Research FDA cooperates with other agencies in research on a wide variety of topics including food safety. Research is joint, collaborative, or funded by other agencies. CFSAN cooperates with the CDC, USDA, NIH and DOD(NAVY), the National Aeronautics and Space Administration, the Department of Veterans Affairs, the National Institute for Standards and Technology and other agencies. The research function and ability to collaborate is essential to solving food safety, food technology and epidemiology questions.

Other Cooperative Endeavors

We would like to highlight several special scientific collaborations that have resulted in successful outcomes. Two examples are illustrative:

A) FDA is providing CDC with $190,800 in FY-96 to continue active surveillance of listeriosis in 5 geographic areas with a total population of 15,000,000. The active surveillance project found a decline in incidence of listeriosis between 1986 and 1992 which coincided with: (1) efforts by FDA, CDC, and USDA to

increase publicity about how foodborne listeriosis is transmitted; (2) increased regulatory activity; and (3) publication of recommendations for prevention of foodborne listeriosis. This low level of disease has continued through 1994. It is unclear at present whether the decline is permanent, and as such, continued surveillance in at least a part of the current surveillance area is crucial.

B) FDA and CDC using DNA fingerprinting technology to analyze *Salmonella tennessee* isolates from numerous dry soy- and milk-based infant formulas and other products, the environment, and two ill Canadian infants were able to link the plant environment and products contained within the facility to illness among consumers. This resulted in the recall of powdered infant formulas, medical foods, whole milk powder, nonfat dry milk, ice cream mixes, powdered drink for meal replacement and a powdered supplement for use by lactating or pregnant women, which were dried and/or packaged at the food processing plant.

ADDITIONAL ISSUES

Mr. Chairman, in your letter of invitation you requested that I speak today about FDA's regulatory actions related to the Transmissible Spongiform Encephalopathies (TSEs), and the relationship between *Campylobacter jejuni* and Guillain-Barré Syndrome. While FDA shares responsibility in these areas with other federal and state agencies, we also have important information to provide.

Campylobacter jejuni and Guillain-Barré Syndrome

Campylobacter jejuni is the most common cause of bacterial gastroenteritis in the U.S., causing an estimated 125,000 culture-confirmed and perhaps three million total cases of diarrhea annually. The predominant source of *C. jejuni* infections is raw or undercooked chicken. Poultry is regulated by the United States Department of Agriculture. Among the commodities which FDA regulates, *C. jejuni* outbreaks in the U.S. are primarily associated with the consumption of raw milk. Other foods regulated by FDA demonstrated to serve as vectors (rarely)

for the dissemination of *C. jejuni* include mushrooms, raw or poorly cooked fish, and raw shellfish (mussels and oysters).

Guillain-Barré syndrome can appear as a late developing illness following a *C. jejuni* infection. It may also follow illness caused by other bacterial pathogens, viral infections, immunizations, major surgery, and other (unknown) causes. The syndrome is characterized by acute neuromuscular paralysis in both adults and children. It develops one to three weeks after an acute respiratory or gastrointestinal infection. It is rare (only about four to five thousand cases per year) and most patients fully recover.

Research/Analysis - FDA conducts applied research on methods to quickly and accurately recover and identify *C. jejuni* in commodities under our jurisdiction. The FDA Bacteriological Analytical Manual contains a chapter on the "Isolation of *Campylobacter* Species from Food and Water." FDA Field Laboratories perform analytical tests for the presence of *Campylobacter* spp. in food commodities regulated by the FDA. To date, we have detected *C. jejuni* in only one sample of shellfish

collected from a shellfish growing area that had been closed to harvesting.

Consumer Education - In a 1991 issue of FDA Consumer, FDA outlined ways to prevent foodborne illness in the home, including prevention tips on safe storage of food items, the importance of cleanliness, the need to keep hot foods hot and cold foods cold, and organisms that can cause disease and their likely source. Other information on *C. jejuni* and its relationship to seafood is available through the FDA Seafood Hotline. The Hotline is available 24 hours a day, seven days a week.

Retail Practices--Guidance - The 1995 *Food Code* published by the Food and Drug Administration serves as guidance to local, state, territorial, and tribal authorities, and to federal agencies in enforcement of their food safety laws covering, restaurants, food stores, institutional feeding, and vending operations. The 1995 *Food Code* includes specific poultry and seafood cooking advice and a consumer advisory regarding the risk associated with the consumption of raw or undercooked animal foods.

Prevention - The prevention of campylobacteriosis relies upon the avoidance of cross contamination in food-handling, maintenance of good kitchen hygiene, adequate cooking of meat and poultry, and the avoidance of those foods known to be vectors. Pasteurization is an effective way to eliminate *Campylobacter jejuni* in milk because the organism is sensitive to heat.

On May 2, 1990, FDA approved the irradiation of poultry up to a dose of 3 kGy for pathogen reduction. Treatment of poultry with radiation had been shown to be effective in significantly reducing the load of several pathogenic microorganisms on poultry products, among them, species of *Salmonella*, *Yersinia* and *Campylobacter*.

Other Activities - CDC, USDA, and FDA have initiated a pilot diarrheal disease reporting system. Working in cooperation with state health departments, CDC will collect and analyze illness data from five "Sentinel Sites" around the country (California, Connecticut, Georgia, Minnesota and Oregon). Data collected will provide a framework for identifying current and emerging trends in foodborne illness. The survey will collect data on diarrheal diseases (including campylobacteriosis) associated with dairy

products, fruits, vegetables, and seafood, which are regulated by FDA, and with meat and poultry, which are regulated by USDA.

Food safety goals are part of the PHS program, Healthy People 2000: National Health Promotion and Disease Prevention Objectives. One of the goals is the reduction of infections caused by key foodborne pathogens including *Campylobacter jejuni*.

Transmissible Spongiform Encephalopathy

Transmissible Spongiform Encephalopothies (TSEs) are a group of transmissible, slowly progressive, degenerative diseases of the central nervous systems that are invariably fatal. Scrapie in sheep and goats, bovine spongiform encephalopathy (BSE), transmissible mink encephalopathy, chronic wasting disease of deer and elk, and Creutzfeldt-Jakob Disease (CJD) in humans are examples of TSEs. The agents believed to be responsible for transmitting TSEs are highly resistant to procedures that modify or destroy nucleic acids of living infectious organisms.

FDA has been active in the trying to understand TSEs. Since 1988 when UK scientists discovered an epidemiological link between

rendered ruminant products in cattle feed and BSE, FDA has participated in BSE discussions nationally and world-wide to understand the agent and epidemic. Collaborations with such organizations as CDC, USDA and NIH have helped the Agency focus on appropriate actions.

USDA has confirmed that no cases of BSE have been diagnosed in the United States. However, as a means of helping to prevent the occurrence of BSE in the US, FDA issued a proposed rule (PR) on August 29, 1994. The PR declared specified offal from adult (more than 12 months of age) sheep and goats as not generally recognized as safe (GRAS) for use in ruminant feed. Since the PR issued, the Agency has evaluated the comments submitted on the proposal and monitored the scientific advances made in understanding the interrelationships among the animal TSEs.

Epidemiological evidence from the United Kingdom (UK) suggests that an outbreak of BSE may be linked to feeding of ruminant proteins to cattle. BSE has been diagnosed in over 155,000 head of cattle from almost 33,000 herds in the UK. A UK ban on the feeding of ruminant protein to ruminants is believed to have resulted in a steady decline in the number of cases of BSE.

Ten cases of CJD with a new neuropathological profile have been identified recently in the UK. Although sporadic cases of CJD occur world-wide at a rate of 1-2 cases per million population per year, these 10 cases appear to represent a new variant of CJD (v-CJD), which might be unique to the UK. The appearance of these 10 cases of v-CJD raises the possibility that they could be causally linked to BSE. However, a link with BSE cannot be confirmed on the basis of this epidemiological evidence alone.

Because of this potential association, an advanced notice of proposed rulemaking (ANPRM) will publish imminently in the Federal Register announcing that FDA is soliciting comments on the issue of using protein-derived from ruminants in ruminant feed. The Agency believes that this action will better protect the health of animals and minimize any risk which might be faced by humans. FDA will be soliciting comments on all aspects of the ANPRM, including, among other things: 1.) the occurrence in the United States of TSEs in animals, including BSE; 2.) how TSEs occur and are spread among animals, and among humans and what vectors might be involved; 3.) scientific information on the ecology of TSEs; 4.)scientific information supporting the exclusion of any ruminant-derived proteins from the proposed

prohibition; 5.) establishment of Hazard Analysis Critical Control Points (HACCP) for the rearing of ruminants, and the rendering or other processing of ruminant derived feed ingredients, that could reduce the need to prohibit the feeding of ruminant protein to ruminants; and 6.) details of rendering or processing practices that may inactivate the TSE agents, and information and evidence of the effectiveness of rendering in the inactivation of TSE agents.

In addition to TSEs and *Campylobacter*, you have asked that I speak about the effect that regulatory delay may have on food safety. The agency currently faces a greater number of challenges and stresses than ever before. New food processing and packaging technologies, new food distribution and consumption patterns, increasing public health concerns about low levels of certain chemical contaminants, and new microbial pathogens all contribute to today's food safety challenges. The size, diversity, and international character of the food industry add to the stress on FDA's food safety assurance program as well, with FDA's current inventory listing over 49,400 food establishments. The number of foreign food products shipped to food products to the United States is continuing to increase. In

1995 alone, there were well over 1.3 million food import entries.

Given the current constraints on government resources, it is unlikely that FDA will ever have sufficient resources to inspect, sample, and analyze more than a small percentage of all food products, domestic as well as imported. Thus, it is FDA's goal to use our resources in the most effective way to minimize consumer exposure to unsafe products. The Agency is developing and implementing new and innovative strategies to meet these goals, through partnerships, improved product review and approval processes, HACCP, reduced number of regulations and environmental assessments.

FOOD ADDITIVE PETITION PROCESS

Mr. Chairman, we would like to take this opportunity to highlight some of the activities that have taken place with regard to the agency's food additive petition process since we last testified before the Subcommittee on this issue and to announce several changes to be made to this process. As you know, on June 22, 1995, the Interim Deputy Commissioner for Operations, Ms. Linda Suydam, testified before this Subcommittee on the subject of food

additive regulation. Ms. Suydam described the changes being made to speed up the food additive review process and additional planned reforms. Since then, we have made some important strides in reducing the petition inventory. I'd like to briefly describe these efforts for you:

At the time of the June 1995 hearing, there were a total of **295** petitions in the inventory. Program staff have made a commitment to have reached a final decision on **at least 100** of these petitions by the end of FY 1996, and I am pleased to be able to report that as of April 30, 1996, **72** of that cohort of petitions have been acted on. (Of course, petitions continue to be received; for example, for the 12 months following May 1, 1995, 56 new petitions were received, and final actions were taken on a total of **82** petitions; of these **53** were approvals. Both of these latter two numbers are higher than for any calendar year since 1986). These gains were achieved because of steps we took during the last year, including:

o reassignment of 23 laboratory scientists to the petition review effort;

o use of the Threshold of Regulation policy, finalized in July, 1995, to exempt from the requirement for a regulation certain low-risk substances used in food packaging;

o increased use of outside scientific experts in resolving novel questions in food additive petitions;

o use of a Special Project Team to expedite review of certain petitions for food packaging materials;

o the dropping or withdrawal of petitions that are incomplete or inadequate.

o establishing objective criteria for judging each employee's performance.

We have also initiated actions that will result in new efficiencies in the process, and further reductions in the petition inventory, including the following:

o We have allocated approximately $1.5 M for the upgrading of information management capabilities to allow modern petition indexing, information retrieval, and document tracking;

o On April 3, we issued a proposal, under the Reinventing Government Initiative, to exempt many petitions from the requirement to prepare an environmental assessment, saving both petitioner and reviewer effort;

o In another REGO initiative, we are preparing a proposal to replace the current lengthy and burdensome GRAS affirmation petition process with a simplified and streamlined notification process;

o We are exploring new ways to improve the quality of submitted petitions, for example, by holding workshops for petitioners, and by making guidance for petitioners more readily available through the World Wide Web;

o Finally, on April 19, we issued requests for proposals for two contracts for review of certain petition data, that will materially assist us in clearing the inventory of unreviewed studies; we anticipate that this action will ultimately have the greatest single impact on inventory reduction of any of our initiatives.

I am convinced that by following through on these initiatives, we will substantially reduce the pending petition inventory to the point where a newly submitted petition can receive the prompt attention of reviewers in all necessary disciplines; only then can we make real progress in improving timeliness and predictability of action on all new incoming petitions. To that end, I am personally following closely the progress being made in

reducing the inventory: weekly, I am receiving regular reports, and will, in the next few weeks, be working with the CFSAN to establish more ambitious performance goals and measures for inventory reduction, and will be looking at any opportunities to provide additional resources for this effort.

At the June 1995 hearing, Chairman Shays noted that the statutory timeframe for review was 180 days, and that any review period in excess of that was in violation of the statute. Mr. Shays urged FDA to deal forcefully with the overdue petitions and requested FDA to suggest a new statutory timeframe that was achievable in practice.

In response to that request, FDA began a comprehensive review of its food additive review program. The results of this review were summarized in a concept paper that was submitted to the Department of Health and Human Services on October 2, 1995. The reform ideas outlined in the concept paper have been discussed with Subcommittee staff, and have, in addition, been the springboard for numerous discussions with representatives of interested food-industry and consumer groups.

FDA proposes a number of substantive changes that would significantly improve its food additive petition review performance, thereby achieving predictable and significantly faster petition reviews. A number of these changes would require amendments to the FD&C Act, and several others would require that new regulations be promulgated or that existing regulations be amended. Today I will describe in detail only the suggestions for statutory changes.

The primary recommended statutory change is that the present 90-day statutory time frame for petition approval (extendable for an additional 90 days) be changed to a:

6-month statutory time frame for conducting complete reviews (extendable for an additional 6 months) for food contact material (so-called "indirect additive") petitions; and

12-month statutory time frame for conducting complete reviews (extendable for an additional 12 months) for so-called direct food additive petitions.

These deadlines will be phased in and become effective over a five-year period. FDA's ability to achieve these statutory requirements and meet these timeframes will depend on reasonable flexibility to reallocate existing resources or development of new external resources, in conjunction with our initiatives to increase efficiency of the process.

By "complete review," FDA means that at the end of the specified time period, the agency will have completed the technical and scientific review and will have either made a decision that the petition is approvable and published a regulation, or has informed the petitioner that the petition is not approvable and the reasons that it is not. The petitioner would have the right to appeal a decision to deny a petition. These deadlines could be extended at the petitioner's request (if, for example, the petitioner prefers an extension to a denial).

These suggested statutory timeframes recognize the fact that some petitions are scientifically more complex than others and, therefore, require longer review. This fact was also recognized in the December 21, 1995, report of the Committee on Government

Reform and Oversight on the food additive petition review process.

I should add an important note: There is currently no distinction between direct additives and food contact materials in the statute. This distinction would need to be established by regulation.

Phased implementation of performance goals

As noted earlier, FDA proposes to phase in its accomplishment of these deadlines over the next 5 years. FDA has already begun to act to reduce the backlog, and will continue to work toward its goal to eliminate the backlog within two to three years. Once the backlog is significantly reduced, FDA's goals are as follows:

For food contact material petitions, FDA's goal is to act on 60% of new petitions within 6 months in the first year of implementation of the new program; 75% of new petitions within 6 months in the second year; and 90% of new petitions within 6 months in the third and subsequent years.

For direct food additive petitions, FDA's goal is to act on 50% of new petitions within 12 months in the first year of implementation of the new program; 65% of new petitions within 12 months in the second year; and 80% of new petitions within 12 months in the third and subsequent years.

Additional recommended statutory changes

FDA recommends that additional statutory changes be made to direct the establishment of new appeal procedures, to streamline rulemaking procedures, to exempt food additive petition review from certain provisions of the Federal Advisory Committee Act and to amend section 721 of the Act to provide for parallel changes for color additive petition review.

Necessary administrative changes

Several other reforms will be needed in order for FDA's overall goals to be met. Perhaps most important among them is the promulgation of regulations to raise the threshold for filing petitions. Such regulations will improve the completeness and

overall quality of petitions, which in turn will increase the likelihood that petitions, once accepted by the agency for review, will be approvable. In addition to the REGO proposals, mentioned earlier, other reforms are also contemplated, among them a requirement that petitioners certify that the data contained in a petition have been properly and correctly recorded, analyzed, and reported.

Likely outcomes of reform in the absence of additional resources

In FDA's June 1995 testimony, the agency committed to improve its food additive review performance without the benefit of additional resources. The reforms identified in the testimony and those discussed above will strengthen FDA's ability to speed petition reviews, and will go some distance toward structuring a workable program of food additive review. However, FDA anticipates that, unless the quality of the petitions it receives is significantly improved, many petitions will not be considered sufficient for filing, and many filed petitions will be denied because they contain unresolved safety questions. This is an outcome that both FDA and the food industry wish to avoid.

These points deserve amplification. With current resources, FDA is unable to devote sufficient resources for consulting with prospective petitioners before filing, because to do so would divert resources needed to review pending petitions. Without pre-filing consultation, and with a new filing threshold that sets higher standards for the information that petitions must contain, many submitted petitions are likely to be found insufficient for filing. For petitions that are filed, the situation is similar. With current resources, FDA is not able to devote the level of effort required to complete all scientific reviews and resolve all safety questions for filed petitions within a time period satisfactory to industry or to FDA. While this cooperative process has added significantly to the likelihood that petitions ultimately will be approved, it has also added significantly to the time required to approve petitions, contributed significantly to development of the present overly long average review times, and has therefore ultimately worked to the detriment of the goal of timely reviews. Were FDA to commit to new statutory deadlines to reach a decision within 12 to 24 months for direct food additive petitions, FDA scientists would be unable to continue their current practice of working substantively with petitioners to resolve the scientific

issues and safety questions that arise during review. If required to reach a decision by the statutory deadline, it is likely, therefore, that FDA would deny many petitions as containing insufficient data to support approval.

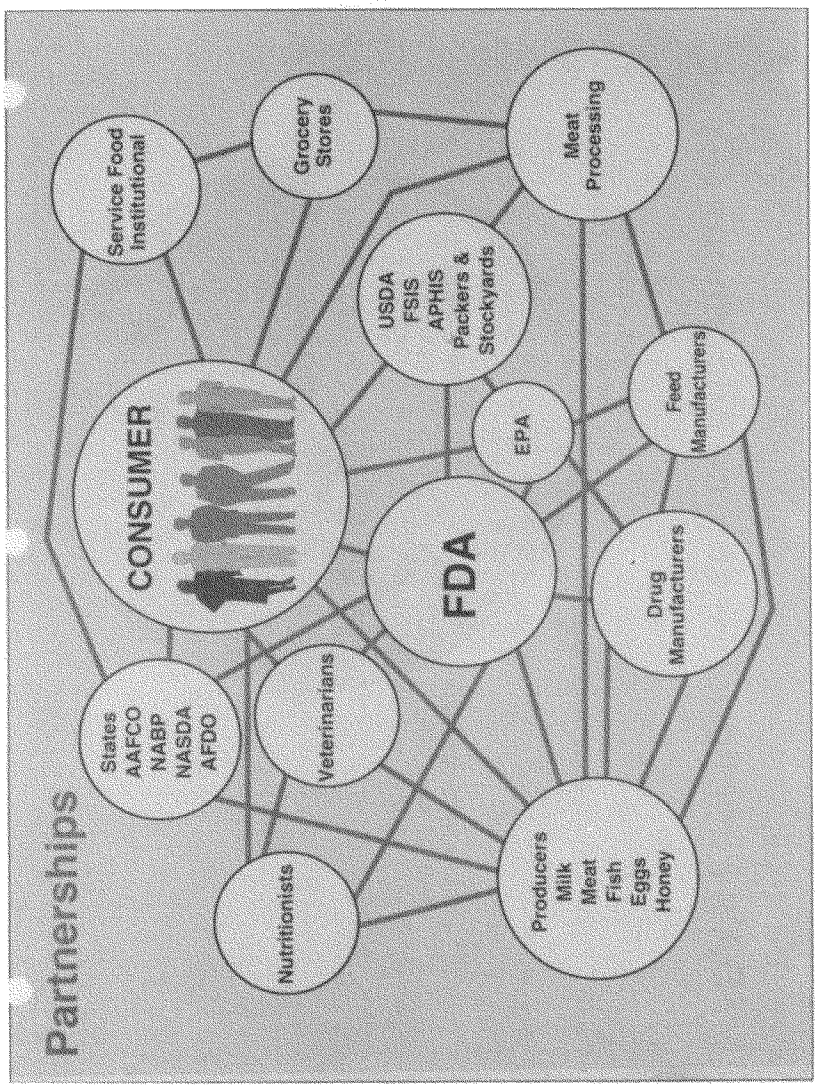
CONCLUSION

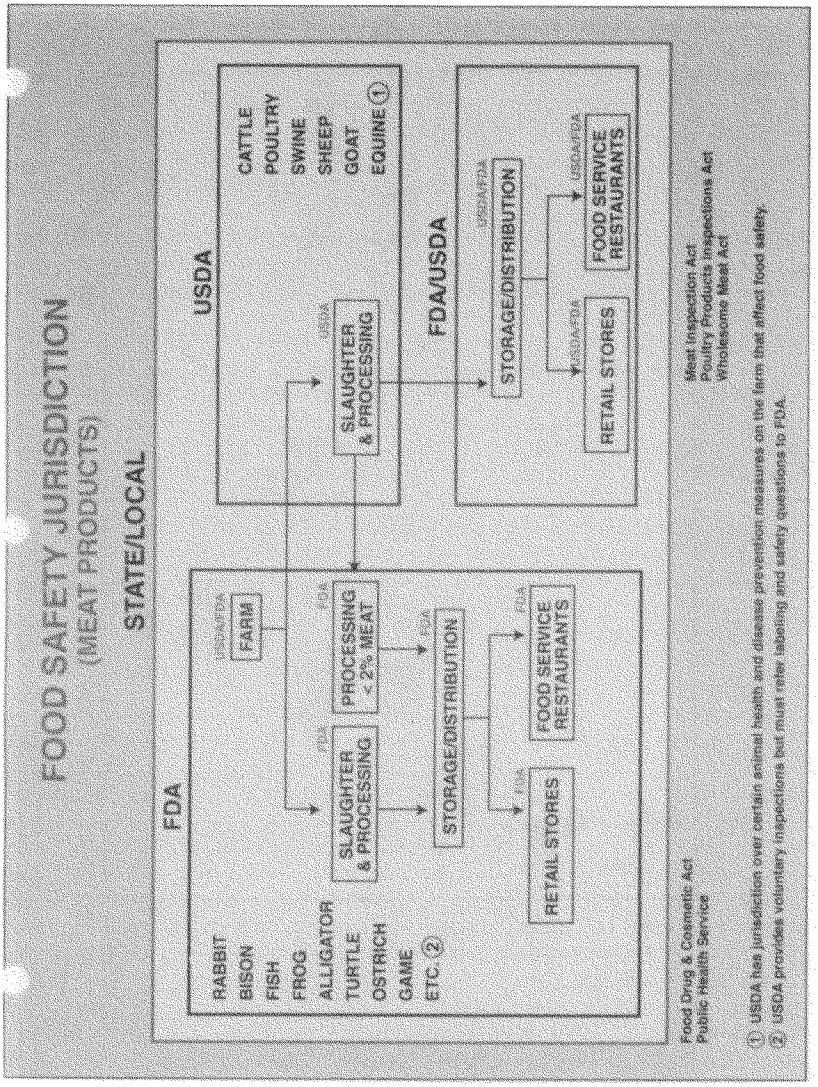
The American food supply is among the safest if not the safest in the world. This has been achieved by incorporating the best science available in our regulatory research, by monitoring, and by education. Changing technologies, rapidly emerging and virulent pathogens, as well as globalization of the food supply present new and unique challenges to maintaining a safe food supply and protecting the consumer. FDA cannot do this alone and indeed has not - but in this time of decreasing resources, as outlined above, we are forming new partnerships, as well as strengthening others with our federal, state, and local counterparts as well as academia and industry to leverage our resources and capitalize on the needs and expertise of our counterparts and customers. These cooperative efforts also include a review of how we currently do business and how best to carry out our mission. As mentioned above, we have made changes

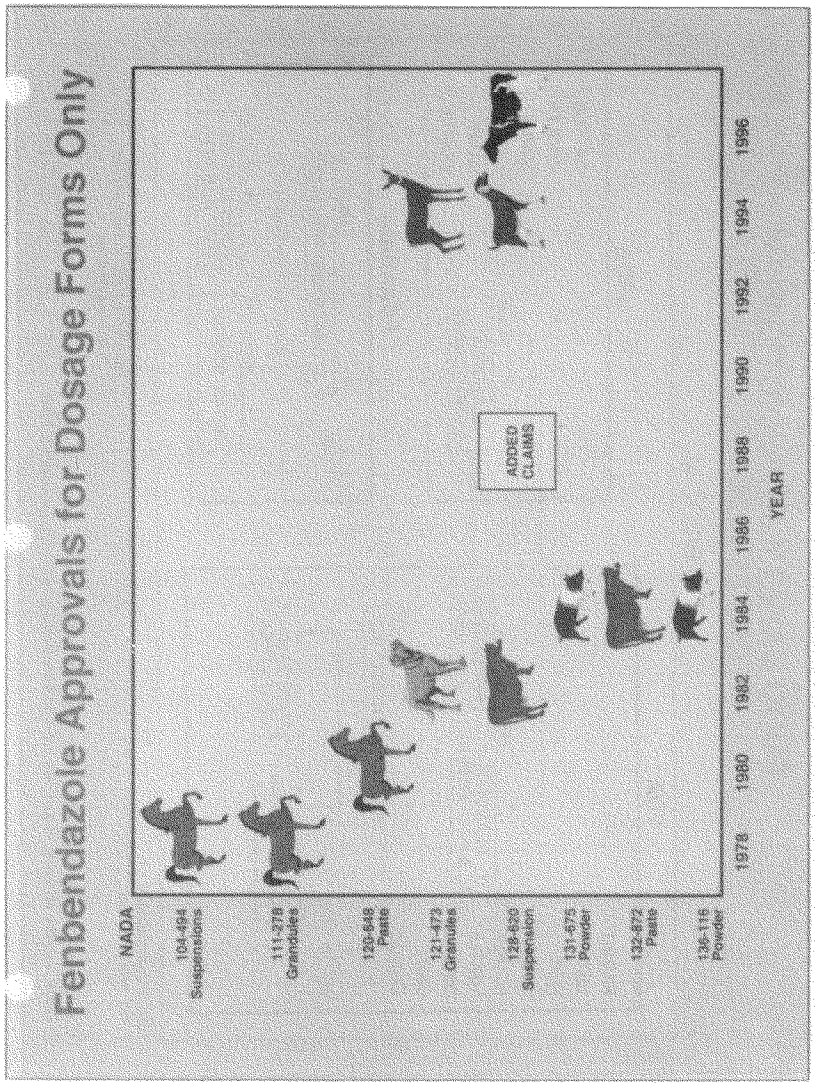
such as in our new animal drug review process and will make changes in other areas to improve the way we function.

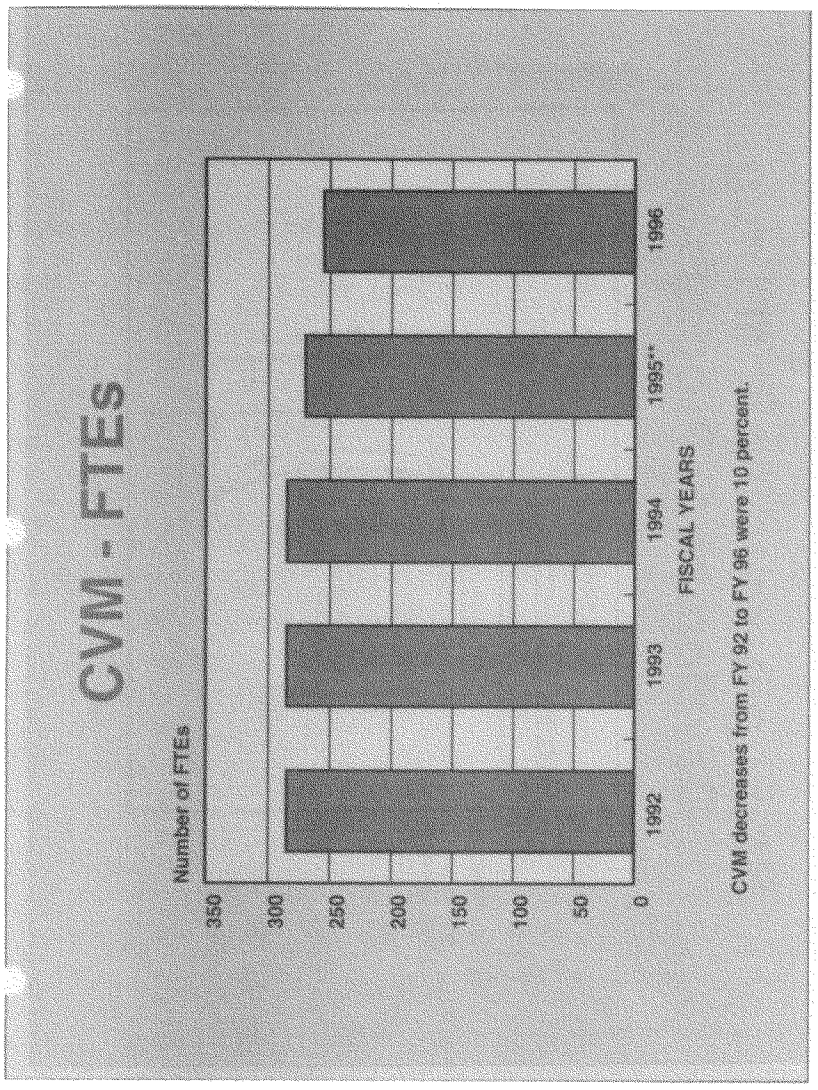
Thank you.

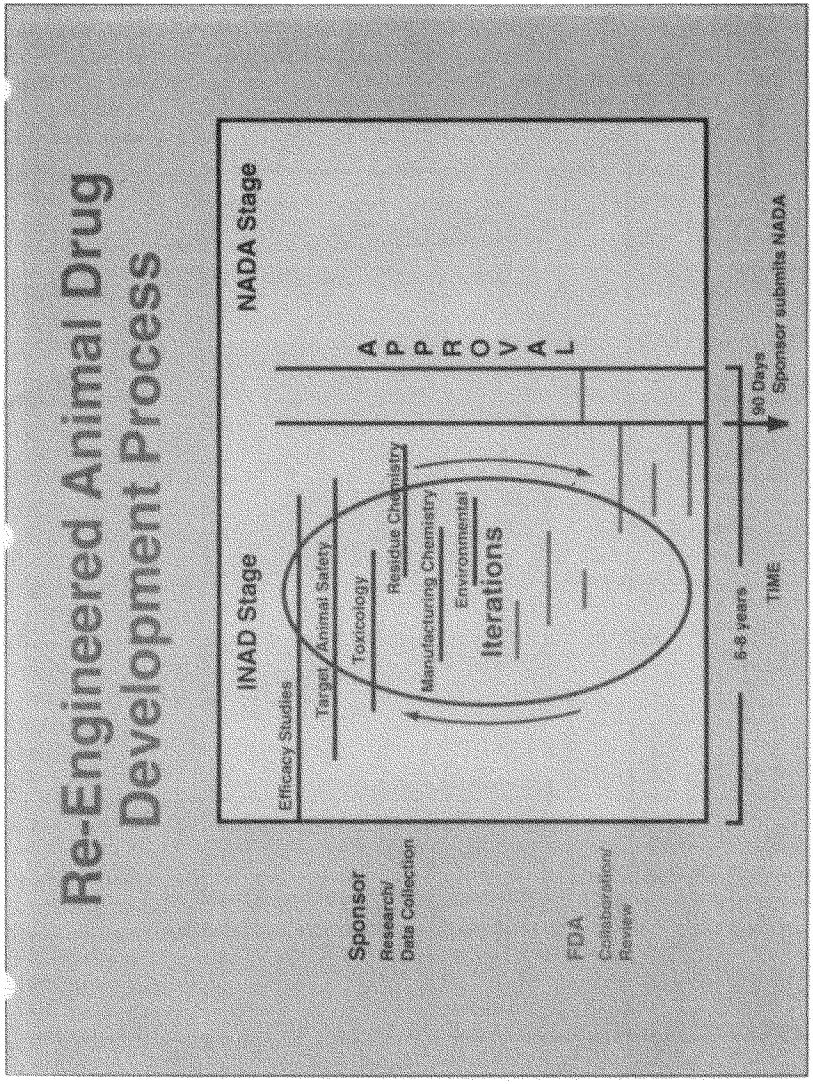
FDA's Functional Resource Allocations (FY 95)
AGENCY POLICY/
PROGRAM DIRECTION 5%
EDUCATION/LIAISON
7.7%
LABORATORY TESTING/
SAMPLE ANALYSES
10.7%
PREMARKET
REVIEWS
24.2%
APPLIED
RESEARCH
14.8%
COMPLIANCE
ACTIVITIES
16%
INSPECTIONS
22.6%

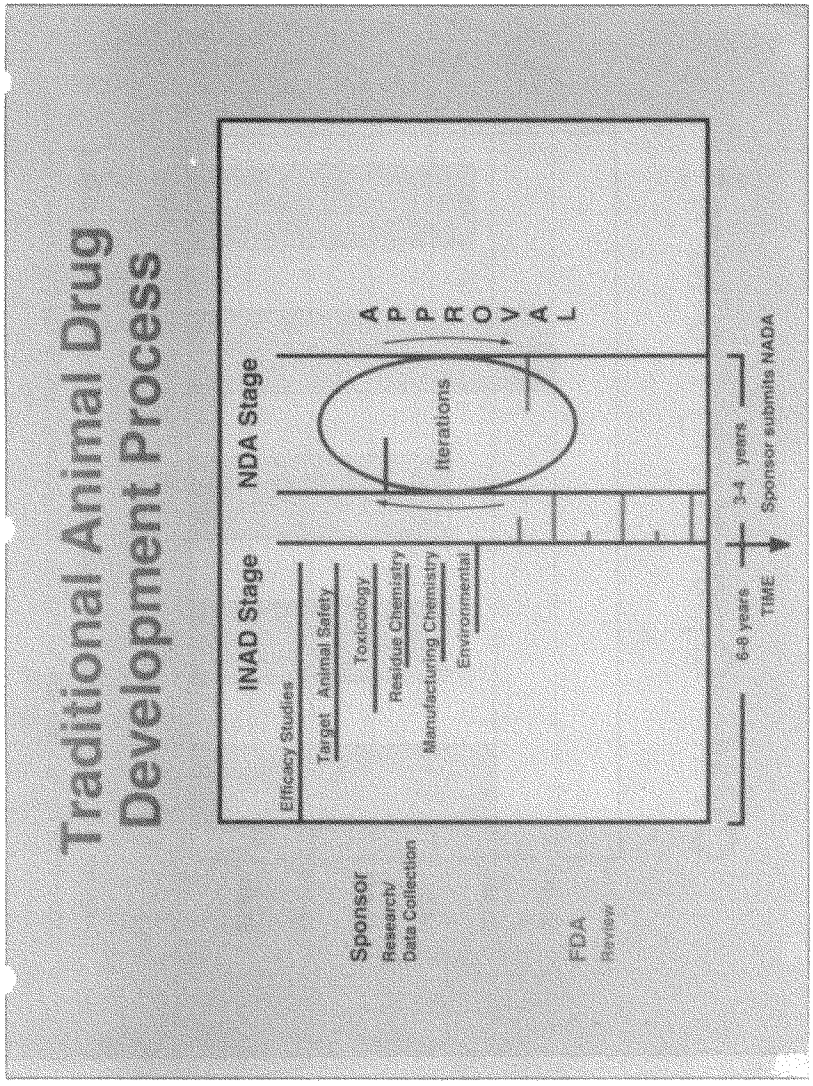

Partnerships
States
AAFCO
NABP
NASDA
AFDO
Service Food
Institutional
Grocery
Stores
CONSUMER
USDA
FSIS
APHIS
Packers &
Stockyards
Meat
Processing
Nutritionists
Veterinarians
FDA
EPA
Feed
Manufacturers
Drug
Manufacturers
Producers
Milk
Meat
Fish
Eggs
Honey


FOOD SAFETY JURISDICTION
(MEAT PRODUCTS)
STATE/LOCAL
FDA
USDA
FDA/USDA
RABBIT
BISON
FISH
FROG
ALLIGATOR
TURTLE
OSTRICH
GAME
ETC. ②
FDA/USDA
FARM
FDA
SLAUGHTER & PROCESSING
FDA
PROCESSING < 2% MEAT
FDA
STORAGE/DISTRIBUTION
FDA
RETAIL STORES
FDA
FOOD SERVICE RESTAURANTS
USDA
SLAUGHTER & PROCESSING
CATTLE
POULTRY
SWINE
SHEEP
GOAT
EQUINE ①
FDA/USDA
STORAGE/DISTRIBUTION
FDA/USDA
RETAIL STORES
FDA/USDA
FOOD SERVICE RESTAURANTS
Food Drug & Cosmetic Act
Public Health Service
Meat Inspection Act
Poultry Products Inspections Act
Wholesome Meat Act
① USDA has jurisdiction over certain animal health and disease prevention measures on the farm that affect food safety.
② USDA provides voluntary inspections but must refer labeling and safety questions to FDA.


Fenbendazole Approvals for Dosage Forms Only
NADA
104-494
Suspensions
111-219
Granules
120-648
Paste
121-472
Granules
128-630
Suspension
131-675
Powder
132-872
Paste
136-116
Powder
ADDED CLAIMS
1978
1980
1982
1984
1986
1988
1990
1992
1994
1996
YEAR


CVM - FTEs
Number of FTEs
350
300
250
200
150
100
50
0
1992
1993
1994
1995**
1996
FISCAL YEARS
CVM decreases from FY 92 to FY 96 were 10 percent.

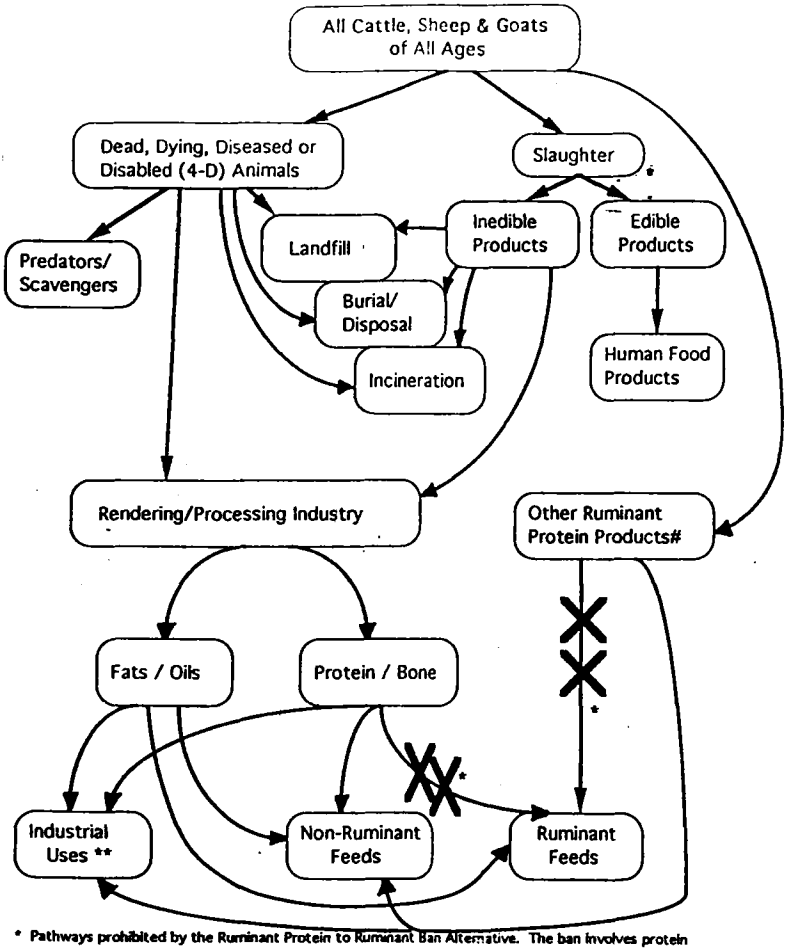

Re-Engineered Animal Drug Development Process
INAD Stage
NADA Stage
Efficacy Studies
Target Animal Safety
Toxicology
Residue Chemistry
Manufacturing Chemistry
Environmental
Iterations
APPROVAL
Sponsor
Research/ Data Collection
FDA
Consideration/ Review
6-8 years
TIME
90 Days
Sponsor submits NADA


Traditional Animal Drug Development Process
INAD Stage
NDA Stage
Efficacy Studies
Target Animal Safety
Toxicology
Residue Chemistry
Manufacturing Chemistry
Environmental
Iterations
APPROVAL
Sponsor
Research/ Data Collection
FDA
Review
6-8 years
3-4 years
TIME
Sponsor submits NADA

CVM - Operating Dollars*
$7,000
$6,000
$5,000
$4,000
$3,000
$2,000
$1,000
0
MILLIONS
1992
1993
1994
1995**
1996
FISCAL YEARS
* Does not include $45 million for the construction of CVM's new laboratory facility.
** Most of FY 95 increase was for the upgrade of computers for the CVM review function.

Effect on CVM's Operating Budget
Of FDA's Protecting Parts of the Budget
Dollars in Millions
5
4
3
2
1
0
1992
1993
1994
1995
1996
1997
1998
1999
2000
Fiscal Years
Budget with Protections
Budget with no Protections

Average Months to Approval
For NADA and ANADA Originals
60
50
40
30
20
10
0
1988
1989
1990
1991
1992
1993
1994
1995
Fiscal Years



* Pathways prohibited by the Ruminant Protein to Ruminant Ban Alternative. The ban involves protein products derived from ruminants of all ages, e.g., lambs, veal calves, feedlot cattle, etc.

*Includes, but is not limited to fertilizers and lubricants.

\# Includes milk products, recycled ruminant waste, dehydrated food waste, dehydrated paunch product, dehydrated garbage. See AAFCO for definitions.

Figure 3. Disposition patterns for ruminants in the U.S. - Ruminant Protein to Ruminant Ban Alternative

Mr. SHAYS. Mr. Towns. All three are prepared to answer questions.

Dr. FRIEDMAN. Yes sir, that's correct.

Mr. TOWNS. Thank you very much, Mr. Chairman. Let me sort of phrase it this way. And I want you to answer—I want you to just walk me through it, using no big words, using no tricky phrases. Just walk me through it very slowly, through the premarket approval process for veterinary drugs. Give me the whole description, how you do it.

Dr. FRIEDMAN. We'd be delighted to do that. Because we found this so complicated, sir, actually, what we did was prepare a couple of charts to try and make it a little bit easier.

Mr. TOWNS. Walk me slowly.

Dr. SUNDLOF. Thank you very much. The animal drug approval process unfortunately is fairly complex, but we've broken it down into really six technical sections. And those are listed up there. The sponsor, the pharmaceutical company, has to prove that the drug is effective. It has to be safe for the animal that it's intended for use in. There has to be—if it's a food animal, there has to be human food safety data that are generated, so that residual drug that may be in the food animal at the time when that animal is eaten or products from that animal is eaten will be safe for the public.

So, therefore, we need to have mechanisms for detecting those drug residues in food producing animals.

We have manufacturing chemistry, as in any drug approval process. This is for the quality to make sure that we have standards of quality for the types of drugs that we approve.

And there is an environmental impact assessment that must go along with the entire package that will lead to approval. Now, this is a very time consuming, resource intensive endeavor to generate the kinds of studies that are needed for drug approval. It generally takes, on average, about $20 million in 10 years to bring a drug for an animal through the approval process. This is less than human drugs considerably, but it still is a sizable investment in time and resources for the companies.

Traditionally, we have asked the companies to develop all of these data over a period of, again, 5 to 6 or 6 to 8 years as approximately the time it takes for companies to generate the data. After they generate all of the data, then they submit the data to the Food and Drug Administration. And we spend time then reviewing. This is generally thousands of pages of materials that we're asked to review. And this takes some time.

Following the review, then, if you look at the chart, the review time is the blue bars on the chart. Notice that after a period of time—and that's a 180 day period—we may ask the company some questions about the submission that we've just reviewed. There may be deficiencies. There may be questions that they have not adequately answered for one reason or another. Or we may have additional questions. Because it is a complex process, it's virtually impossible to get everything right the first time. And that requires additional review cycles. We ask the companies for additional information. They provide us back additional information. And that also is on a 180-day timeframe.

So there may be several cycles that actually lead up to the final decision. And the final decision in most cases is approval of the drug. In some cases, it is disapproval of the drug. That is in a nutshell the process by which we review and approve new animal drugs.

Mr. TOWNS. I thank you very much, Dr. Sundlof. Mr. Chairman, I'm prepared at this time to break and come back and continue the questioning.

Mr. SHAYS. It will probably take us about 15 minutes. I don't think it will take us longer, but we'll come back about 25 of, maybe a little sooner. We stand at recess.

[Recess.]

Mr. SHAYS. The hearing will come to order. Mr. Towns.

Mr. TOWNS. Thank you very much, Mr. Chairman. And thank you for walking me through. Now, in a followup, where in the approval process that you describe is the 180-day marker?

Dr. FRIEDMAN. Thank you, Mr. Towns. Let me just follow up, if I may, with what Dr. Sundlof began. And I can show you where the 180 days period of time are. If we can go to the previous one, please, Bob. Thank you.

The requirement for answering questions at each point in time, we must act within the 180 days, so that if new information is submitted to us, the requirement is that we must respond to the sponsor, either say, this is fine or this is not fine, or we need something else. But we can't extend past 180 days to do that.

Let me step back from that for a moment and try and deal with your first question, which is: What's the meaning of the 180 days, anyway? A hundred and eighty days is a very important benchmark in trying to get to an end point. The end point is providing the best information that we can to someone who is going to be using a product. So that we're able to review information about a new product, decide if it's safe, if it's effective, what the side effects are, what kinds of animal diseases it helps. And we want to do that in as fast a time as we can consistent with getting all of the information.

So in some situations, we're able to do this quite rapidly when a very good proposal has been submitted to us. In other situations, it's a much more tedious and time consuming process.

If I may just show you one thing, sir, and I promise not to take more than a moment. This was the old process, the traditional process that Dr. Sundlof explained, with all of the questions and answers going on inefficiently late in the process. Bob, if you could just show that.

The system that's been re-engineered, if you will, by the Center for Veterinary Medicines, under this situation, the time is compressed considerably, because a lot of the questions and answers go on while the data are being generated. So that if questions arise, they can be dealt with in a very timely manner. That means that when the application is completed, the time to finish reviewing it and the time for approval can be very, very short.

An example of that is a recent product which, after all of these iterations of questions and answers, it took only 22 days to get a product finally approved. That's what we're shooting for, sir, is to do this in a much more timely way.

Mr. TOWNS. So by that time, is your agency compliant with the statute, would you say? Do you feel that you're in compliance with the statute?

Dr. FRIEDMAN. I would say, sir, for in excess of 90 percent of the products, that is true. There are some products for which we have exceeded the 180-day limit. And we're working hard to reduce that to as close to zero as we can. But in the majority of products, yes, sir.

Mr. TOWNS. Let me just move to another area, because I'm concerned about budget cuts. And I think that sometimes we are so anxious and eager to get involved in budget cuts that we can create problems for agencies.

Since 1990, Congress has added to the responsibilities of the FDA while providing almost no resources, very little resources. Today, 25 cents of every dollar is spent on products regulated by the FDA.

Has the speed with which animal drug and feed applications are processed been affected by the broad scope of the FDA's regulatory responsibility?

Dr. FRIEDMAN. It's a very important question, sir, and I guess I would answer it in the following way. The agency at this moment is under three sorts of constraints or considerations. The first is the unprecedented amount of new scientific information which affects all of our reviews and all of our approvals. Today we're talking about food safety in veterinary products, but it's equally true for devices or drugs or human biologics.

As the science becomes more complex, the reviews become more difficult. So that's one concern, is that American science has been fabulously productive. Now, we're getting the translation of basic science into practical knowledge.

The second is that expectations for the agency's performance are high and getting higher. And the public, not just consumers, but industry, congressional oversight, everyone expects the FDA to perform in a better way. And I must say to you, sir, that no one has higher expectations for the FDA than we do ourselves.

The third is that there are limited resources and that, both in terms of personnel and dollars, it is a matter of competing priorities between different parts of the agency at any one moment as to how those responsibilities are best discharged. This is something that we must be very vigilant of, we must be very careful of, to look and see that we don't neglect important components of our areas of responsibility. But it's constantly a balancing act.

Mr. TOWNS. Thank you very much. I see the clock and my time has expired.

Mr. SHAYS. You can keep going.

Mr. TOWNS. Thank you very much, Mr. Chairman. I understand that more than 50 percent of FDA's activities are in food regulation. Is that correct?

Dr. FRIEDMAN. No, sir. That's not exactly correct.

Mr. TOWNS. What percent would you say is in food regulation?

Dr. FRIEDMAN. If one looks overall at food safety and food approval activities, it's about one quarter of the agency, about something in excess of $200 million. The figure that has been quoted, about 50 percent, has to do with certain inspectional requirements.

We take inspections of food institutions very seriously. Please, I don't mean to be misunderstood on this. But it is only a component of what the agency does. A more accurate figure is something closer to the 20 to 25 percent range, sir.

Mr. TOWNS. But isn't it true that the operating budget declined by at least 50 percent over the past 4 to 5 years?

Dr. FRIEDMAN. No, sir, that's not quite correct, either. If I may, could I please have chart No. 8, please? Thank you.

The base budget, the budget projection at the beginning of the year for the Center for Veterinary Medicine did show a decrease. But each year, the agency has added to that base to have the following sorts of dollar figures over the period of 1992–96.

In 1994, there was an additional bonus of money given, especially to deal with some computer and information resources, because we know that's critical to the processing of new applications. If we're going to speed that along, we need the infrastructure to do it.

So that, in fact, I certainly recognize that that is not exactly a completely level operating dollar figure. But it does not demonstrate a trend of decreasing.

Mr. TOWNS. Well, let me put it this way. Would you say that CVM has been treated fairly in this process?

Dr. FRIEDMAN. My ability to make philosophical judgments like that is somewhat limited, sir. I think if I may generalize and say, at any time in the agency, there are far more good ideas and far more legitimate needs than we have resources to manage at any one time. This is a competition of priorities. I think some of the most important and some of the most valuable contributions of CVM have been supported. But I'm sure that Dr. Sundlof would certainly list for you other things that he would like to pursue. But there are certain limitations that we must accommodate.

Mr. TOWNS. Let me then ask Dr. Sundlof. For the record, please indicate in FTE's, the number of primary reviewers actually dedicated to the following types of products, applications for this year, and what you project for fiscal year 1997 in terms of new animal drug applications, abbreviated new animal applications, supplemental new animal drug applications, and animal food additive petitions.

Dr. SUNDLOF. Thank you, Congressman Towns. I will give you some broad answers right now and we will be able to submit additional, more specific figures for the record, if that is all right.

Mr. TOWNS. Mr. Chairman, I'd like for the record to remain open for additional information.

Mr. SHAYS. Fine.

[The information referred to follows:]

Specific Figures to Supplement the Record at Page 26 of Draft Transcript:

Mr . Towns: FOR THE RECORD PLEASE INDICATE, IN FTEs, THE NUMBER OF PRIMARY REVIEWERS DEDICATED TO THE FOLLOWING TYPES OF PRODUCT APPLICATIONS FOR THIS YEAR, AND WHAT YOU PROJECT FOR FISCAL YEAR 1997 NEW ANIMAL DRUG APPLICATIONS; ABBREVIATED NEW ANIMAL DRUG APPLICATIONS; SUPPLEMENTAL NEW ANIMAL DRUG APPLICATIONS; AND ANIMAL FOOD ADDITIVE PETITIONS.

Response: The following table gives most of the statistics requested in the question; however, in some cases we have provided more information than requested in order to give a clear picture of the review process. Specifically:

- We have not provided a separated break-out of NADAs and NADA supplements, because the same reviewers normally work on both and it is a continuously changing mix.
- We have provided a number for INADs which was not requested, but since this now accounts for the major portion of the review resources we thought it was an important piece of the picture.
- We have not included a projection of the FY 97 numbers, because we are still uncertain as to what the FY 97 budget will be, and at this point, it would be very speculative.

Submission Type	FTEs for FY 96
New Animal Drug Applications	22.8 *
Investigational New Animal Drugs	67.9 *
Abbreviated New Animal Drug Applications	4.9
Animal Food Additive Petitions	3.7

* As noted in bullet two, above, under the phased review process a major portion of the technical review of the data occurs during the INAD stage of product development.

Dr. SUNDLOF. Thank you. We have approximately 109 people that are engaged in the review of new animal drug applications. About 90 of those people are actual review scientists. And the other 18 are support personnel. Their full-time position, their full-time job is to review new animal drug applications or generic animal drug applications. We don't separate those out into separate categories.

Now, through the streamlining of Government, we have taken reductions in our total number of employees, as has the rest of the agency. We have tried to preserve the review function. And up until this year, we have not taken any reductions in the area of premarket review of animal drugs.

This year, we can no longer maintain the current rate at which we have been staffing that, because other parts of the Center are suffering. But to the extent that we possibly can, we are making the review of animal drugs our highest priority in the Center.

Mr. TOWNS. The reason I am raising these questions is that when we talk to people in industry, they always talk about the fact that certain information doesn't flow, certain applications are not processed, certain things don't move. And they say, well, you know, they're doing a good job up there, but there's a lack of resources. I mean, they almost apologize for you.

So I'm concerned about that. We're fighting hard enough to make certain that we have the necessary tools to do the job that needs to be done. And that's the reason why I keep pushing into this line of questioning. And I also recognize that sometimes it's very difficult for you to say some of the things that you might want to say. I understand that, too. I've been around here now a few years. I didn't get here yesterday. I was here last week, I mean.

But I think that somewhere along the line we need to begin to make this case if this is the problem. And I am sort of more and more beginning to feel that this is the problem. Additional resources are needed in order to do some of these things in a timely fashion. And that's the reason why I want you to know I keep asking this information.

But let me put it this way. Maybe all of us will feel a lot more comfortable if I say it this way. What should we do on this side? Tell me what we should do on this side. And maybe that makes everybody a little more comfortable. And that includes telling the chairman what he should do, too.

Dr. SUNDLOF. If I may answer that?

Mr. SHAYS. Please.

Dr. SUNDLOF. Thank you. Because we know we're not facing additional resources, that's Government in general, and we're willing to accept that. We're looking for different ways of making our process more efficient. And some of those can be done internally that we can do through rewriting our regulations to improve the efficiency, which we are doing. Other things are going to take some statutory changes.

We're trying to introduce a new category of drugs for feed, animal feeds this year. But we lack the statutory provisions to do that. That would be the veterinary feed directives.

We would like to have the ability to establish tolerances on drugs that are not approved in this country, but are major trading part-

ners. They may be extremely important for their countries. They may have diseases that we don't have in this country. And yet we wouldn't be able to declare their product safe unless we have the authority to grant import tolerances.

We want to move away from a lot of the paperwork that we're doing with registered feed mills, such that they don't have to have a license for every single drug that they mix. We'd like to license the entire establishment. But that will take a statutory change.

We would like to have greater flexibility in how we declare a drug to be effective. So the effectiveness standards need to be adjusted to make them more commensurate with the way drugs are really used in this country. And to allow us to have a regulatory environment in which small market drugs can make it through the approval process. But that would require a statutory change in some of the efficacy standards.

We would like to provide more flexibility in how we approve drugs in combination. Much of our agriculture depends on using more than one drug in the feed. The feed is the only vehicle that they have to get drugs into animals. Yet, under our present statute, it makes it very difficult. And we don't think that that adds a lot of value. So we would like to see some changes in there.

Finally, we would like to have some changes in the way we approve drugs for relatively minor species, the ones for which there is no market: gold-fish, pets, endangered species; emerging industries, like aquaculture, that is going to be very important to this country. And those are all things that the Congress can certainly help support. And we are working with our industries to try and come up with changes that we think are in the best interest of the public.

Mr. TOWNS. Thank you very much. I must admit a lot of that makes a lot of sense to do it, to come up with those changes. And I look forward to working with you because I really feel that the time here in terms of we need to look at this very seriously. And whatever it is that needs to be done, I think we need to address it. We're talking about safety, and I understand that, and we want to make certain that there are no problems.

But at the same time, I really feel we can do better. There is no doubt in my mind that we just sort of need to address it and do better.

So, Mr. Chairman, thank you very much for the time.

Mr. SHAYS. Thank you, gentlemen. I'm going to have a number of questions. Some of them will be quite general. And some of them you will say, why did he ask that, because you're so familiar with the issues. But, first, I have a sense that your agency will become more important to Americans over the years to come.

In the past we basically looked for physical, visible manifestations of problems that are more easily detectable. And that now with pathogens and so on and with what has been happening in the last 10 or 20 years, the inspection process becomes quite different.

Dr. FRIEDMAN. It's a very good set of questions and very complicated, as you point out. The Food and Drug Administration has been devoted to looking for more efficient ways of ensuring the safety of the food supply. So, although some visual inspection has

been important, we have actually pioneered some techniques for rapid, in the field assays for bacteriologic contamination or for other sorts of toxin contamination.

Our seafood program is, I think, especially noteworthy in that regard. But I don't mean to limit it to that.

I think that looking at the entire spectrum from the production of the animal to the provision of the food at the grocery store and even to how the consumer uses that food and prepares that food, those are areas that we've been engaged in and that greater science is being brought to that.

So, as you point out, visual inspection is necessary, but far from sufficient.

Mr. SHAYS. I guess really what I'm asking is with diseases like *Campylobacter* and *listeria* and *E. coli* 0157, did they exist before, we just didn't really recognize them?

Dr. FRIEDMAN. If I may take the example of *Campylobacter*. This is an organism that exists normally and is not a pathogen. It doesn't cause disease in poultry, in cows. It's a widely distributed organism in certain animals. And it is incredibly sensitive to heat, so that if food is properly prepared, it really doesn't cause any problems.

Mr. SHAYS. I guess the question I'm asking, though, are we creating new challenges now? Did they always exist? We just never recognized it?

Dr. FRIEDMAN. I think two things. One is that we are much better at identifying diseases now than we ever have been. So part of it is increased sophistication and diagnosis.

The second, though, is a real sense that there are some changes in bacteriologic flora and how we deal with that, how humans deal with it.

So it's two things, one of which is a better appreciation. And as you recognize, the Centers for Disease Control, the USDA, a number of other important sister agencies or sister organizations in this help oversee and overview that entire spectrum.

Mr. SHAYS. When we got into the issue of the safety of the blood supply, we get the general sense that we're dealing with new challenges that we never had to deal with before and that we have to have new defenses and new processes to detect contamination of the blood supply. And I'm wondering if I can just make the same analogy to the area that you're involved in.

Dr. FRIEDMAN. I think that's correct. There is one additional thing. And that is that, instead of just being the passive recipients, we're actually active in this regard. By that, I mean we have concerns about how microbes change their sensitivity or resistance to antibiotics that we currently have. And so the widespread use of antibiotics in people changes the microbiology of the bacteria.

We're looking carefully to see whether the widespread use of certain anti-infective agents changes the bacteria in animals that may affect humans. So we're actually part of this whole scheme, as well, in a way.

Mr. SHAYS. The whole issue of animal drugs and medicated feeds, your two responsibilities.

Dr. FRIEDMAN. Yes, sir.

Mr. SHAYS. Which takes more of your resources?

Dr. FRIEDMAN. I would ask Dr. Sundlof to answer that.

Dr. SUNDLOF. Well, let me just say that medications are approved. They're approved as drugs for animal feeds. Following the approval, then the feeds are regulated. The individual feed mills are inspected that mix the drugs in the feed.

We spend the majority of our money—and I can give you a more exact break-down at a later date. But the majority is spent on the preapproval side of it, so the drug side, before they're approved. And then the surveillance and enforcement of the Medicated Feed Program is less. I can't tell you how much less, but we invest less money in that part than in the preapproval side.

But we get a lot of cooperation. We multiply our resources by engaging the States and helping us in the inspections of the medicated feed.

[The information referred to follows:]

Supplemental information for the Record beginning on page 34 of Draft Transcript:

Mr. Shays: COMPARE THE COST OF THE NEW ANIMAL DRUG REVIEW PROCESS WITH THE COST OF THE ANIMAL FEEDS PART OF THE PROGRAM.

Response: The new animal drug review process including the review of NADAs for animal drugs to be used in making medicated feeds, as well as, the review of animal food additive petitions, the field inspectional component, and pre-market compliance functions uses approximately 221 FTEs while the animal feeds part of the program uses approximately 20 FTEs. In addition to the other areas mentioned above, the new animal drug review estimate also includes Center and Agency management. The animal feeds estimate includes FTEs located in the Division of Animal Feeds, as well as, small numbers of FTEs from the compliance, human food safety, environmental, field inspectional, and Center and Agency management functions.

Mr. SHAYS. The States meaning the industry or the State regulators?

Dr. SUNDLOF. No, the State regulators.

Mr. SHAYS. And we regulate in all 50 States? I mean, is the regulation process primarily Federal or State?

Dr. SUNDLOF. It is primarily Federal. We regulate in all 50 States, but in approximately 21 States, we have contracts with the State regulatory officials to inspect feed mills.

Mr. SHAYS. So they function on your behalf?

Dr. SUNDLOF. Yes.

Mr. SHAYS. I didn't ask this. I do want you to give me a sense in terms of your personnel that we would follow up on and in terms of your resources. What area of these two represents your biggest concern, the area that you feel you need to focus the most amount of your attention on right now?

Dr. SUNDLOF. The two areas being personnel and what else?

Mr. SHAYS. No, animal drugs versus medicated feeds.

Dr. SUNDLOF. They're inextricably linked. You cannot separate those two.

Mr. SHAYS. I've been just trying to understand. The reason why we call it the mad cow disease is that we don't want to say a word that has no meaning to us. But, obviously we don't want to link what has happened to Great Britain to what is not happening in the United States. But—and it's not a "but." What interests me is if we did have an indication in the 1980's of what was happening in Great Britain and not knowing the answers to these questions, why are you announcing this morning that you're starting to look at the ruminant issue and say that it's going to be regulated?

I want to be clear what that means. In other words, is the issue now that they have to prove it safe, whereas before they could assume it was safe and you had to prove it wasn't safe?

Dr. SUNDLOF. Yes, I believe it's correct.

Mr. SHAYS. Would you say it in your words?

Dr. SUNDLOF. Sure. Let me answer the first part of your question. The Center and the agency have been working with other organizations to track scientific information about mad cow disease for a number of years. And we certainly have since the late 1980's and early 1990's indicated in various ways to different parts of the industries that we regulate, our concern and their need to be vigilant and careful about mad cow disease.

The ban on feeding one ruminant protein to another ruminant was first——

Mr. SHAYS. Let me just be clear in my understanding of the issue.

Dr. SUNDLOF. I'm sorry.

Mr. SHAYS. The whole concept of ruminant is that we're basically saying these are animals that have more than one stomach and that somehow this has an impact over what, retaining certain what?

Dr. FRIEDMAN. You're quite right. Ruminants have four stomachs. And commercially what we're talking about are goats, sheep, and in the United States, beef is the largest number of animals.

The transmissible diseases, the transmissible spongiform encephalopathies can, in fact, affect a whole lot of different animal species. They don't just affect ruminants.

The reason that this is such an important consideration is that as part of animal feed, beef and sheep can be processed and rendered into food product protein for other beef or sheep presumably.

Mr. SHAYS. High protein.

Dr. FRIEDMAN. And that the concern from the United Kingdom was that there was a sort of cycling. That you had infected tissue that was then fed to a cow or some other animal. In this case, a cow. That wasn't infected, but might become infected.

This has not been completely proven, but I think the majority of evidence is very suggestive of this. And that's the reason why we think it appropriate to look very carefully—not just we, but the World Health Organization and others—to banning this protein feeding.

Mr. SHAYS. What I'm trying to understand now, though, is the level that you're bringing this to and your decision today to basically, what, regulate it? Are we basically saying there is an assumption that you have to prove it's not safe and now there is an assumption that the industry has to prove it's safe? Walk me through this and be very clear.

Dr. FRIEDMAN. I will certainly try to. And I'll ask others, if I don't make it sufficiently clear, to please help me in that regard. Currently, there is concern that because feeding ruminant-to-ruminant may represent a health hazard, that this can no longer be considered safe and therefore must be regulated.

We are asking in the advance notice of proposed rulemaking on display today, we're asking for scientific and other sort of information that would help craft the very best proposal. The World Health Organization has made a sort of blanket ruminant-to-ruminant ban, but they haven't been very specific about what that means. We're trying to both complement and expand that recommendation that they've made.

Mr. SHAYS. Let me just be very candid here. They made that kind of announcement in the late 1980's.

Dr. FRIEDMAN. No, sir, I don't believe so.

Dr. SUNDLOF. April of this year.

Dr. FRIEDMAN. It was April 1996, I believe, sir. We can get you that information.

Mr. SHAYS. Let me ask you this. When did we become concerned about what might be happening in Great Britain? When did the world community start becoming concerned?

Dr. SUNDLOF. From the animal standpoint, we were concerned as soon as the disease was identified.

Mr. SHAYS. And that was in the 1980's?

Dr. SUNDLOF. That was in the 1980's.

Dr. FRIEDMAN. Yes, sir, 1986.

Mr. SHAYS. So walk me through there. The issue that presents itself to me is that we had a concern about the blood supply obviously with HIV and AIDS. There was a concern. But we didn't act on that concern in a quick way. And almost every hemophiliac became HIV infected. And then we woke up to it. And I just want to be comfortable. What action did the United States take from

1986 to now in more general terms? What action did we take as a result of an early warning sign?

Dr. FRIEDMAN. Well, your question is——

Mr. SHAYS. And I'm going to say something else to you.

Dr. FRIEDMAN. Please.

Mr. SHAYS. There was concern when we had this hearing by different Members of Congress, one, that we not have this hearing; and by different people in the industry that we not have it because we didn't want the media to make it more than the problem it is.

But at the same time, we don't want to make it less of a problem. So I'd like to have you walk me through what we've done since 1986.

Dr. FRIEDMAN. I'd be happy to, sir. The situation that you compared to the blood supply could not be more different. Let me just be very clear about that. Your concerns about the blood supply are absolutely appropriate. And I understand where those concerns arise. It could not be a more different situation here.

The Food and Drug Administration has been integral and has been deeply involved in information and considerations about BSE. But it would be inappropriate for me to try and represent the full breadth of all of the agencies that have been involved in this, because a large answer to your question comes from the U.S. Department of Agriculture. They have been a prime moving force in both the evaluation, the scientific evaluation and regulation of protecting the United States from importation of feed.

Mr. SHAYS. So one of the things we did was we made sure that no cattle were imported from Great Britain. And that would have been a USDA action.

Dr. FRIEDMAN. That's correct, sir. So I can't—one of the things I'm trying to do is to give you a sense of how broad the activities have been and how our ability to speak to only a portion of that shouldn't be misconstrued as either fragmentation, because it's not.

Mr. SHAYS. Well, that was one of the problems we encountered with the blood supply.

Dr. FRIEDMAN. Right. But, sir, not having the CDC and USDA and other people who have been integrally involved in this makes it difficult to put together a coherent story.

Mr. SHAYS. Fair enough.

Dr. FRIEDMAN. And I want to answer your question really well. I would be happy to tell you what the Food and Drug Administration did and can certainly go through that with you.

Mr. SHAYS. Let's do that.

Dr. FRIEDMAN. The recognition of the disease first in the late 1980's in the United Kingdom, there was a period of time when it wasn't so clear what the cause of the disease was. And lacking that information made it difficult to recommend how one would prevent the disease or control the disease. But that in addition to the bans taken by USDA, it did become more apparent and it did become more logical that the feeding of infected sheep with the disease called scrapie, which is somewhat like the BSE, was in fact suspicious for being linked.

That information, though, was not translated into a ban in this country for a couple of reasons; one of which was that there was no BSE in this country. Again, this is something that the U.S. De-

partment of Agriculture would have to give you more information on.

Mr. SHAYS. Have we established whether it jumps from species to species, BSE and scrapie and so on? I mean, is that still an open question?

Dr. FRIEDMAN. I think it depends. The reason I'm hesitating is this is an area of intense biologic investigation, with a lot of controversy and a lot of confusion. It is possible to transmit from one kind of animal to another this disease. For example, you can take some tissue from an infected animal, inject it directly into the brain of another animal. But many times when you try and do that experiment, it fails. Sometimes it succeeds.

The exact cause of the disease is still under a lot of investigation.

Mr. SHAYS. So there is still a lot of uncertainty.

Dr. FRIEDMAN. A tremendous amount of uncertainty, yes, sir.

Mr. SHAYS. So far, I do see parallels to the whole issue of the blood supply. We knew there was a problem. We didn't know what it was. There was uncertainty and so on. I mean, I do see similarities. I guess what you're trying to tell me is that the agencies involved are working together in this issue where they didn't maybe work in a coordinated way.

Dr. FRIEDMAN. Well, I certainly would say that. But the second thing is that, again, I'm really reluctant to push the analogy. But there was HIV disease diagnosed in the United States before the blood supply was known to be infected. There has been no BSE disease in the United States. And I think that's really—this is a difficult analogy and I'm reluctant to push it further.

Mr. SHAYS. What would be the issue in regards to TSE's?

Dr. FRIEDMAN. TSE, transmissible spongiform encephalopathies, is like an umbrella term, a generic term for including things like human Creutzfelt-Jakob Disease or the mad cow disease or scrapie or minor species disease where this has been seen. It's a general descriptive term.

Mr. SHAYS. We have no scrapie in this country?

Dr. FRIEDMAN. Again, sir, this is a question that I feel much more comfortable with you asking the Department of Agriculture. My understanding is there is scrapie in this country. That there is not very much scrapie in this country and there aren't very many sheep as compared to Great Britain. But, again, this is not an area that we regulate or that we have intimate knowledge of.

Mr. SHAYS. I don't know why that makes me uncomfortable. Why wouldn't you, since we have to deal with the issue of ruminants, why wouldn't that be something that you would be involved in?

Dr. FRIEDMAN. In the regulation of sheep, sir?

Mr. SHAYS. We're talking about the question of whether we use the parts of animals, correct?

Dr. FRIEDMAN. Yes.

Mr. SHAYS. And we use it as feed?

Dr. FRIEDMAN. Yes.

Mr. SHAYS. That it may spread the disease. And isn't that your area?

Dr. FRIEDMAN. No, no, it certainly is, sir. But the point I wish to make is that's an area where we work closely with the U.S. Department of Agriculture in order to ask the questions of: How much

infection is there? How is the rendering being done? Where is it being processed?

Mr. SHAYS. Let me get back to your regulation that you're doing today. Explain to me again what you are doing, what you are announcing today. Let me just say that we appreciate this announcement being made today as opposed to tomorrow so we can ask you about it. But there is a part of us that wonders why today and not a month earlier or 2 months earlier and so on. It's just important. I'm happy you're making this announcement. I just want to understand it.

Dr. FRIEDMAN. Sure. And if I may, the reason that we announced it today is that I couldn't announce it any sooner in terms of moving as quickly as we thought would be possible.

Mr. SHAYS. What are you announcing today?

Dr. FRIEDMAN. The Food and Drug Administration is soliciting comments on the issue of using protein derived from ruminants in ruminant feed. We point out that the association of the various TSE's. And then we say, this action is being taken to protect the health of animals and to reduce any risks which might be faced by humans. FDA is requesting scientific and economic information and other comments relating to the prohibition of ruminant protein and ruminant feed.

Mr. SHAYS. Let me ask a dumb question. You could have taken that information months ago, couldn't you? I don't understand why you couldn't have made that decision sooner.

Dr. FRIEDMAN. I'm sorry. The decision to ask for information?

Mr. SHAYS. Yes.

Dr. FRIEDMAN. The World Health Organization issued their recommendation on—what date was it, Steve?

Mr. SHAYS. Why would it take the World Health Organization to tell us to do something?

Dr. FRIEDMAN. I think, sir, the question was—since we had already proposed a sheep ban earlier, we saw——

Mr. SHAYS. A sheep what?

Dr. FRIEDMAN. A sheep ban. That is, we had proposed in 1994 the prohibition of using certain parts of sheep in ruminant feed.

Mr. SHAYS. Right.

Dr. FRIEDMAN. It became increasingly clear that that was neither scientifically or clinically sufficient because as information was being developed, that cattle being rendered in cattle feed might also be a cause of transmissions.

Mr. SHAYS. That's not really helpful to me because I don't feel——

Dr. FRIEDMAN. I'm sorry, sir, please.

Mr. SHAYS [continuing]. I know you're trying to be cooperative; I just want to have this down. Let me ask parenthetically: We don't know about what parts of an animal may be causing the problem, if in fact it is causing a problem; is that correct?

Dr. FRIEDMAN. We have a suspicion that some parts, such as brain and certain organs are much more likely.

Mr. SHAYS. So it's conceivable that you might end up saying you can use certain parts, but not other parts of an animal?

Dr. FRIEDMAN. That's one of the things we're wrestling with, yes, sir.

Mr. SHAYS. All I'm trying to understand is—and I feel like we're digging deeper into a hole I don't want to get into. But you're digging the hole. I don't understand the statement that says to me that you couldn't have done it sooner when all I hear you asking for is for people to report to you.

Dr. FRIEDMAN. No. I'm sorry. Let me be a little bit clearer if I may on this. We're asking for scientific information to help craft what the ultimate regulation will be. We're doing this at an accelerated——

Mr. SHAYS. That you could have done a year ago.

Dr. FRIEDMAN [continuing]. We did this for sheep. We did not do this for beef.

Mr. SHAYS. My point is you could have done it a year ago.

Dr. FRIEDMAN. Right.

Mr. SHAYS. I mean, whether you should have, but you could have done it a year ago.

Dr. FRIEDMAN. Practically, yes, sir. It would have been possible.

Mr. SHAYS. There is no practical reason why you couldn't.

Dr. FRIEDMAN. Yes.

Mr. SHAYS. So now is that the only thing you're announcing today? What will that lead to? Just walk me through it.

Dr. FRIEDMAN. Let me, if I may, take one step back. The background into which all of this is occurring is the announcement of a voluntary ban that the beef industry has made that they themselves recognize that there may be some risks and that they're prohibiting the use of ruminant in ruminant feed. They're recommending that. What will take place today is the announcement that we wish to have more information, especially more scientific and economic information.

We're asking that within 30 days, that information come to us. We will then utilize the information to craft a more definitive proposal. We would like to, within the next few months, complete work on that and have that published in a final form.

Mr. SHAYS. Final or proposed?

Dr. FRIEDMAN. In the next few months, in a final form. This is an announcement of a proposed. We will have the proposed regulation, I hope, shortly thereafter, as short as we can after.

Mr. SHAYS. I don't know what short means.

Dr. FRIEDMAN. Well, 30 days for the comment period. There is some economic assessments that are required by law that we're working on very vigorously right now. We hope to have all of that information put together.

Mr. SHAYS. Let me just conclude by saying, my information says—and I'm going to read it. In 1991, the World Health Organization recommended that, "In BSE free countries where the relevant risk factors are present, e.g. use of ruminant protein in ruminant feed, the occurrence of scrapie, the size of the sheep population relative to that of cattle, et cetera, consideration might be given to the exclusion from ruminant feed of selected tissues that contain higher hydrates of the agent."

Now, that's 1991.

Dr. FRIEDMAN. Yes, sir.

Mr. SHAYS. Not 1996. What's the difference? What am I confused with?

Dr. FRIEDMAN. What you're confused with there is the term, consideration, might be given, depending upon the factors of the numbers of sheep and the numbers of sheep involved. For example, I believe I'm correct in this in saying that in the United States, 0.02 percent of the feed is sheep.

Mr. SHAYS. So the difference is that this was sheep versus the cattle?

Dr. FRIEDMAN. Yes, sir.

Mr. SHAYS. And our sheep population is relatively small or very small?

Dr. FRIEDMAN. It is relatively smaller. And the amount of sheep protein in animal feed is relatively small. And so the risks, we think, tend to be commensurately small.

Mr. SHAYS. Mr. Towns, do you have another question or two?

Mr. TOWNS. No, I'm fine.

Mr. SHAYS. Let me just say this. Dr. Shank, we haven't asked you any questions, which probably is good, huh? But I'd be happy to have any of the three of you just make some points that you think you need to make before we call our next panels. And do you think you need to clarify anything, because we don't want to leave anything unclear. I'd like to make sure that's on the record, as well.

Dr. FRIEDMAN. Maybe just to reiterate the one point that you raised in your initial remarks, sir. And that is, the safety of the supply, of our food supply is something that we're all very proud of. But it would be arrogant, it would be inappropriate for us to assume that that will continue without very dedicated efforts on not just the part of the Food and Drug Administration, but all of the other relevant bodies. We take that very seriously.

Mr. SHAYS. I do know you take that very seriously. And we take our function very seriously. And this is very candidly a new territory for us. I guess that's quite obvious. But this is something, I have a feeling whether I'm in the minority and he's chairman or it stays the way it is, this will be something that continues.

Mr. TOWNS. I like that.

Dr. FRIEDMAN. Mr. Chairman, if I could just say one other thing. This is really complicated. And we appreciate that fact. Your staff knows that if we can provide you with further information, just please feel free to call upon us. This is important for you to be well informed and we want to do that.

Mr. SHAYS. Well, it's important for the entire Congress to be well informed.

Dr. FRIEDMAN. Absolutely.

Mr. SHAYS. You are going to get back to us with a breakdown on how your resources are. Dr. Sundlof, do you have anything to add? Dr. Shank, I'd really like it if you would say something. Is there some question we should have asked?

Dr. SHANK. I had my chance last year.

Mr. SHAYS. Is there some question you wish we had asked that we didn't?

Dr. SUNDLOF. I think you covered the points that we think are important. If you ask people in the Center for Veterinary Medicine what their primary concern is, why they're there, they'll tell you it's because of the safety of the food supply. As Dr. Friedman said,

we take that responsibility very seriously. I think you're absolutely right that we are seeing a new era where we're looking more at the emerging diseases that are occurring. And that CVM's role will have to change in the future to be more cognizant and more prepared to deal with those issues of new zoonotic organisms. I think you're absolutely right on target.

Mr. SHAYS. Well, I know this is a concern you have. I also know it's a concern the industry has and should, because obviously they want to have a safe supply and we don't want to have a problem that we could have avoided.

We do have a vote, I think. I do thank our three witnesses. I really appreciate your being here. What we're going to do is if Mr. Towns gets back before I do, he'll swear in the witnesses and we'll start the testimony of our second panel.

Would you put all of your charts in the record, not just the ones that you showed? Is that possible? Do you have hand-outs of other charts, besides this?

Dr. FRIEDMAN. We do.

Mr. SHAYS. How many other charts do you have?

Dr. FRIEDMAN. Three or four.

Mr. SHAYS. Would you put them all in the record? Not the big one. We'll keep the small ones.

[The information referred to follows:]

Below are FDA's responses to a number of additional questions provided in writing to FDA by Mr. Towns on the day of the hearing.

Question 1 THE NUMBER OF FTES (full time staff) IN THE CENTER FOR VETERINARY MEDICINE HAS DROPPED 7% FROM 287 FTEs IN FISCAL YEAR 1991 TO 267 FTEs IN 1995. HAS THIS DECLINE IN STAFF IMPACTED CVM's ABILITY TO PERFORM ITS PRODUCT REVIEW FUNCTIONS?

Response: In the earlier part of this period, up through 1995, the overall reductions were smaller, and the Center was able to take them in overhead activities (such as the Office of Management) and in the Research and Surveillance and Compliance areas. This allowed the Center to protect its product review function. However, in FY96 the continued FTE reductions coupled with a reduction of 17.5 percent in the operating budget went beyond what the Center could absorb in these areas. While the Center's highest program priority is to make more animal drugs available for use by the country's agricultural community, we were forced to reduce our drug review functions. The Center could no longer review compassionate INADs or research INADs. These are two small but important parts of the drug review process. The compassionate INADs were used to allow veterinarians to legally obtain and use not yet approved drugs to treat sick animals. Without review of research INADs, research programs, in particular university programs, either cannot sell animals treated with unapproved drugs or they have a withdrawal period of six months.

During the past few years the Center has re-engineered its animal drug review process in order to reduce the time it takes to get new animal drug products to the market. We are now beginning to see some success from this initiative.

Question 2: THIS PAST JANUARY, THE SUBCOMMITTEE ISSUED A BIPARTISAN REPORT WHICH FOUND DELAYS IN THE APPROVAL PROCESS FOR NEW FOOD ADDITIVES. SIMILAR CONCERNS HAVE BEEN RAISED ABOUT HOW LONG IT TAKES TO BRING A NEW VETERINARY DRUG TO MARKET. THE STATUTE SAYS 180 DAYS -- ACCORDING TO AN FDA GRAPH PROVIDED THE SUBCOMMITTEE, 20 MONTHS WAS AVERAGE IN 1995.

DOES THIS GRAPH ACCURATELY DEPICT PROBLEMS IN CVM'S PETITION REVIEW PROCESS? IN OTHER WORDS, IS YOUR AGENCY NON-COMPLIANT WITH THE STATUTORY REQUIREMENT REGARDING REVIEW OF VETERINARY DRUGS AND FEEDS?

Response: The graph is accurate; however, this does not mean that there are problems with the petition review process or that the Center is non-compliant with statutory requirements.

The complexity of scientific data provided in new animal drug submissions necessitates a thorough review of each application to ensure all animal drugs approved are safe and effective. Any discussion about the timeframe for approval of animal drug applications with the end goal of making more animal drugs available must take into consideration the underlying issue of whether the data submitted to the Agency by animal drug sponsors is adequate to approve the new animal drug application. In most instances, animal drug sponsors have not been able to provide in their initial submission all the data necessary for the Agency to make safety and effectiveness decisions to approve a new animal drug application within the 180 days specified in the statute. That is to say, typically the intial submission is inadequate to support approval. After reviewing an application, the Center notifies the sponsor of any deficiencies in the application including the need for supplemental data. Most sponsors then generate the additional information required and resubmit the application. Typically, two or more such resubmissions, each with its own statutory review time period of 180 days, are needed before the requirements for approval are satisfied.

The Agency is exploring a number of ways to improve the quality of new animal drug applications, including phased review of applications from the INAD stage, and presubmission conferences. The presubmission conference is particularly important because it provides an opportunity for the Center and the sponsor to discuss and come to agreement on the data requirements for a particular NADA at the beginning of the sponsor's data development process. Experience has shown that the use of phased review and/or presubmission conferences has resulted in a substantial increase in the quality of applications submitted to the Center. Consequently, approval decisions can be made more quickly.

Regarding whether CVM is in compliance with the statute, the Federal Food, Drug, and Cosmetic Act provides in section 512 (c) that the Center make a determination as to whether an application can be approved within 180 days or such additional period as agreed upon with the sponsor. In most instances where the Center surpasses the 180 day limit the extension has been made with the sponsor's consent since the extension is usually for the purpose of bringing to closure more quickly a specific issue raised by the application. Thus, the Center generally is in compliance with the Act.

Question 3: CAN YOU DEMONSTRATE WHAT PERCENTAGE OF THE AVERAGE 20 MONTHS APPROVAL PERIOD IS ATTRIBUTABLE TO CVM AS COMPARED TO THE DRUG SPONSOR?

Response On the average the time is split about 11 months (56%) FDA time and 9 months (44%) industry time.

Question 4: ONCE THE PHASED REVIEW SYSTEM IS FULLY FUNCTIONAL, HOW LONG DO YOU ESTIMATE THAT THE PETITION REVIEW PROCESS WILL TAKE?

Response Once the phased review system is fully functional the Center estimates that it will take less than 90 days to complete the review and administrative processing of an NADA. Most decisions at this stage of the review process should be approvals since most of the issues will have been worked out in the INAD phase.

Question 5: DR. WELSER, WHO WILL BE WITH US ON THE THIRD PANEL, HAS INDICATED IN HIS WRITTEN TESTIMONY THAT THE PHASED REVIEW SYSTEM IS NOT EFFECTIVELY COORDINATED IN ITS FINAL STAGES. HOW DO YOU RESPOND TO THIS CONCERN?

Response We are not certain of the specifics of the concern raised by Mr. Welser in his testimony. However, we would like to say that two of the primary goals of phased review are to ensure that each phase of the animal drug review process is effectively coordinated and to eliminate any second guessing of decisions made earlier in the process. Phased review relies on a team approach where teams consist of reviewers from various disciplines. Each member of the team has the responsibility to keep each other and the team leader appraised of the current status of the application. As with any new endeavor, phased review is a work in progress, and CVM recognizes the need for finetuning. We will continue to work with sponsors to address any concerns they may have.

Question 6: IT WAS NOTED IN THE WRITTEN TESTIMONY OF A PENDING WITNESS THAT ALTHOUGH CVM HAS AUTHORITY OVER THE MANUFACTURING ASPECTS OF THE DRUG APPROVAL PROCESS, THE FDA DISTRICT OFFICES HAVE OVERSIGHT OF THE ACTUAL MANUFACTURING FACILITIES. DOES THIS RAISE PROBLEMS WITH DUPLICATION OF EFFORT AND MISCOMMUNICATION?

Response FDA's District Offices perform on-site inspections to assess each firm's level of compliance with 21 CFR Part 211 Good Manufacturing Practice requirements and to confirm the firm's conformance with 21 CFR Part 514 related to manufacturing processes and controls (e.g. the District Office verifies on-site that manufacturing processes, equipment, and controls reflected in the firm's pre-approval submission to CVM are in place). The District Office then directs CVM's attention to any areas of specific concern when they report the results of their inspection.
We are aware that criticisms of this process, such as those described by your witness, have existed in the past. However, CVM has worked to develop closer ties with the District Offices and the Office of Regulatory Affairs to ensure greater efficiency in the manufacturing aspects of the approval process and to eliminate

any duplication of work or miscommunication. We believe that this approach is working. With closer ties between these Offices, CVM can focus its attention on review of specific areas of manufacturing and controls that are most closely related to the drug approval process.

[Recess.]

Mr. SHAYS. Thank you. The hearing will come to order. We have in our second panel, Dr. Frederick Murphy, School of Veterinary Medicine, University of California, Davis; Dr. Lester Crawford, Association of American Veterinary Medical Colleges; Dr. Gary Weber, National Cattlemen's Beef Association; Dr. Don Franco, National Renderers Association; and Robert Hahn, Public Voice for Food and Health Policy.

For a second there, I thought the only way you got to be on this panel was to be a doctor here.

[Witnesses sworn.]

Mr. SHAYS. Note for the record that all five witnesses have responded in the affirmative. We'll start in the order that I called you, I guess. So we'll start with you. I guess we'll just go right down the line there. That's perfect. Thank you, Dr. Murphy. Nice to have you here, sir.

STATEMENTS OF FREDERICK MURPHY, SCHOOL OF VETERINARY MEDICINE, UNIVERSITY OF CALIFORNIA, DAVIS; LESTER CRAWFORD, ASSOCIATION OF AMERICAN VETERINARY COLLEGES; GARY WEBER, NATIONAL CATTLEMEN'S BEEF ASSOCIATION; DON FRANCO, NATIONAL RENDERERS ASSOCIATION; AND ROBERT HAHN, PUBLIC VOICE FOR FOOD AND HEALTH POLICY

Dr. MURPHY. Mr. Chairman, I'd like to include my complete testimony in the record. The rest of my statement has to do with the organizational structure for food safety in our country.

Mr. SHAYS. Without objection.

Dr. MURPHY. I spent 25 years at the Centers for Disease Control as well as at my present address at University of California, where I ended up as Director of the National Center for Infectious Disease. I'm a virologist. And so I've had a lot of background in human and animal diseases.

As you said earlier, I don't think we need to say much more about the fact that the problems we face today in food safety are quite different than those of years ago. The most recent food-borne disease episodes seem to have stemmed from newly recognized, newly emergent microbes diabolically adapting themselves to our high tech food industries. The case of BSE in Britain is a case in point.

The issue before the committee is driven entirely by the announcement on March 20 of this year that 10 people in the United Kingdom may have become infected with the BSE agent through exposure to beef:

"Although there is no direct evidence of a link"—between BSE and CJD—"on current data and in the absence of any credible alternative, the most likely explanation is that these cases are linked to exposure to BSE before the bovine offal ban in 1989. This is a cause for great concern."

It seems to me that it's necessary to give some background so as to better understand this announcement.

First, there is a need to appreciate the nature of the prions, those infectious agents that cause the spongiform encephalopathies, that is, scrapie in sheep, BSE in cattle, and CJD in humans. Prions

are the most bizarre infectious agents ever. They are infectious proteins, rogue proteins. They have no DNA, no RNA like microbes and viruses. Instead, a normal protein is converted to rogue protein just by contact.

Mr. SHAYS. Is that true for all prions, or just these?

Dr. MURPHY. For all prions, each in its own host species. The rogue protein just contacting normal protein changes it to more rogue protein. And that is done as the protein refolds. It's very weird.

The rogue protein builds up in neurons in the brain and causes severe dysfunction and eventually death. The rogue protein, this abnormally folded prion, is extremely tough. It resists boiling. It resists high doses of radiation and many chemicals. It can even be stored in formaldehyde.

Mr. SHAYS. If you don't mind, I'm just going to interrupt you again. Are prions a new phenomenon or have they always existed?

Dr. MURPHY. The concept of the infectious prion was developed by Stanley Prusiner. It's been evolving over the last 10 or 15 years. In the last couple of years, the concept has become, in my view, fact.

Mr. SHAYS. But, now, scrapie has been in existence for over 200 years.

Dr. MURPHY. Right. But the cause of it as a prion is something——

Mr. SHAYS. The prion. Can you define it or categorize it in that particular way?

Dr. MURPHY [continuing]. Prion has been the concept for at least 10 years, maybe 15. Its voracity and its certainty is in the last few years.

Mr. SHAYS. I'm sorry to interrupt you. This way, I won't have to go back. Thank you.

Dr. MURPHY. So the prion is one tough hombre.

Mr. SHAYS. I can understand that. Can you understand that?

Mr. TOWNS. No question about that. That's clear.

Mr. SHAYS. We should have had this panel first.

Dr. MURPHY. Scrapie in sheep has been present in the United Kingdom for at least 200 years. And offal from scrapie-infected sheep have been rendered into cattle feed for many, many years. In the late 1970's, the rendering process used to make protein supplement and bone meal was changed, leaving out a solvent extraction step. And it's been hypothesized, but not scientifically explained, that the scrapie prion present in cattle feed somehow initiated the formation of the BSE prion.

BSE was first recognized in the United Kingdom in 1986. As cattle sickened and died, their carcasses were rendered and fed back to more cattle, thereby amplifying the epidemic. And in my written testimony, you see the epidemic curve.

By March of this year, there had been more than 161,000 cases of BSE in the United Kingdom involving 59 percent of all dairy herds. And at the peak of the epidemic in 1993, there were more than 1,000 cases a week being reported.

From very early on in this bovine epidemic, questions were asked about human health risks. By 1990, front page articles in all British newspapers over and over were begging this question. Does

BSE pose a risk to human health? And, consistently, British Government officials responded, no, there is nothing to worry about. This, of course, led the public to become more and more skeptical.

And editors of the distinguished British scientific journal, *Nature,* responded 1990: "Never say there is no danger or risk. Instead, say that there is always danger or risk and that the problem is to calculate what it is. Never say that the risk is negligible unless you are sure that your listeners share your own philosophy of life."

In my view, this quote really sums up the central precept of public health practice.

On March 20 of this year, the British Government announcement about the 10 human cases of CJD caused an incredible splash. These cases were unusual in several ways. Eight of the patients had died. Mean age 27, versus mean age 63 in the background CJD that occurs throughout the world, including our country, at a rate of about 1 case per million per year.

The course of disease in these people was longer than usual. And the lesions in the brain were different than usual. Most of the patients presented with psychiatric problems, as well as the usual sign of CJD which is dementia.

Last week, it was announced that 10 more human cases, including three from a single small town, are being studied in the United Kingdom And 2 weeks ago, a single case in a young man in France was announced.

On March 22, the European Union announced an embargo on all imports of beef from the United Kingdom I might say parenthetically that by 1989–90, most other countries in the world, including our country, had issued a similar embargo. No products, no beef, no cattle from England have been allowed into this country since 1989.

The British Government responded by announcing a ban on selling meat from cattle that were more than 30 months of age. They announced a selective slaughter and incineration policy. Public confidence crashed. And the political fall-out has been incredible, escalating each week. The local elections of last week damaged the Tory government tremendously. The British press presaging that as——

Mr. SHAYS. Where are you headed on this kind of testimony, though?

Dr. MURPHY [continuing]. I just want you to know what a big deal this is in Great Britain.

Mr. SHAYS. I think it is a big deal. And your testimony is helpful and it's good to have that.

Dr. MURPHY. I'll move on. You've already stated what the U.S. response has been, and we've heard from FDA what its response has been.

Mr. SHAYS. But I'd like you to state what you think the U.S. response has been, because I'm not quite sure what the U.S. response has been. We basically banned allowing cattle to come in from Great Britain. I'm just not clear on it. So if you want to enlighten me there.

Dr. MURPHY. Our actions and policy up to the time when these 10 human cases were announced to have been described; since

then, the heat has been turned up in this country, too. Three different agencies of the USDA have announced enhanced activities, more surveillance, more education and more research.

In contrast, as you've already noted, the WHO on April 2 announced even stronger recommendations: that all countries must conduct surveillance of cattle and humans; that all countries must adopt compulsory notification of cases, cattle and humans; that all countries must ban all ruminant-to-ruminant feeding; and that all countries must conduct more training.

In my view, a lot of soft comment, rationalization, and even denial has been evident in some quarters all along. In 1995, USDA issued a statement noting, "The incidence of BSE in animals born after the ban in Britain is at a much reduced rate." Note the term reduced rate, not zero rate. "The ban has been effective in reducing the risk of infection." Note again the word "reducing," not eliminating.

As late as 2 weeks ago, I read in British newspapers, which I see on the Internet, statements from British Government officials saying, British beef is safe, can be eaten with confidence, the future depends upon a restoration of public confidence. I see the difference between a report of a disease episode, as you've heard about here, and the issue of a crisis and confidence as quite different and somewhat at the root of the hearing here today.

What about the future of the episode in the United Kingdom? No one can say. Infectious diseases have always been unpredictable. It's very common at this point for people to think that the worst is behind us. In most infectious disease episodes that I've been involved in, that's not been the case.

Will the epidemic in cattle in the United Kingdom absolutely end with the true enforcement of a ruminant-to-ruminant feeding ban? Or will some other transmission pattern, maybe less common but still important, become evident hiding behind this feed-borne transmission pattern? How many more cases of the human variant CJD disease will be found in humans? I said the British announced 10 cases, but they're studying 10 more. How will British public confidence ever be restored?

We can't really answer these questions. The best we can do is design policy very prudently based on expert opinion while at the same time keeping a weather eye on events in the United Kingdom

So this, in my view, is the necessary background and context for the issue of ruminant-to-ruminant feeding and the question of whether it should be banned in our country. There is scrapie and sheep in our country, not an uncommon disease, and it's present in lots of different places, especially in the Midwest.

But there is absolutely no evidence, as has been noted, of BSE in our country in cattle. Therefore, it seems to me that all of our planning has to be preventive at this point. How can we make sure that BSE never gets started in this country?

Banning immediately by one means or another all ruminant-to-ruminant feeding would add an additional level of surety to the present voluntary ban. But in my view, this is only a small step. Whatever the steps beyond expedited rulemaking, as you heard in the first panel, the next steps that move faster do come under the Public Health Service Act. And I'm not an expert on that.

As I said, I think more needs to be done. We've really got to support the kind of research that FDA needs. In my view, FDA's No. 1 need is for a rapid test that can be done on live animals. Over the past few years, we've heard over and over again that such tests, antemortem tests for BSE, are just around the corner. Where are they?

Mr. SHAYS. Could you draw your testimony to a close?

Dr. MURPHY. Yes, sir. Just one last comment?

Mr. SHAYS. Sure.

Dr. MURPHY. And that is that I also really think that FDA needs research so that whole carcasses condemned by virtue of rulemaking can be turned into something other than fly ash by incineration. The Canadian Government is taking the lead in this, in developing superautoclaving systems that would render a carcass into something with some nutritive value. Thank you.

[The prepared statement of Dr. Murphy follows:]

CONGRESS OF THE UNITED STATES
House of Representatives
Committee on Government Reform and Oversight

Subcommittee on Human Resources and Intergovernmental Relations

Hearing: Role of the Food and Drug Administration in Protecting the US Consumer from Food-borne Diseases

Date: May 10, 1996

Testimony of: Frederick A. Murphy
School of Veterinary Medicine
University Of California, Davis
Davis, CA 95616-8734

Longer Text for the Record:

I am Frederick A. Murphy, Dean of the School of Veterinary Medicine, University of California, Davis. Formerly, I was Director of the National Center for Infectious Diseases, Centers for Disease Control & Prevention, Atlanta. I am a virologist with broad experience in human and animal diseases. I am here today because I am concerned about our country's approaches to the prevention of food-borne diseases.

I don't think I need say much about the overall scope of the food-borne disease problems facing our country. If the worthiness of the problems were not recognized, we'd not be here today.

Similarly, I don't think I need say much about the fact that the problems we face today are different from those of years ago—today, the problem does not stem from filth in our processing plants; rather, most recent important episodes seem to have stemmed from the presence in foods of newly recognized, newly emergent microbes, diabolically adapting to our "high tech" food industries. The case of *E. coli* 0157:H7 in hamburgers is a case in point; so is *Salmonella enteritis* in eggs, other *Salmonella* in poultry, and bovine spongiform encephalopathy (BSE, "mad cow disease") in cattle in the United Kingdom.

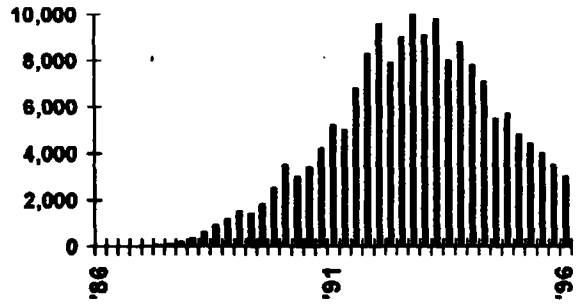
The issue before the Committee here today concerns "ruminant-to-ruminant" feeding—that is, the feeding of processed/rendered offal and other materials derived from sheep and cattle back to cattle in the form of protein supplements and bone meal. The issue before the Committee concerns the questions posed by the BSE epidemic in cattle in the United Kingdom (UK) from 1986 to the present, and the questions posed by the announcement made in the UK on March 20th of this year that 10 people may have become infected with the BSE agent through exposure to beef. The UK's Spongiform Encephalopathy Advisory Committee (SEAC) announced: *"...[discovery of] a previously unrecognized and consistent disease pattern..."—" although there is no direct evidence of a link, on current data and in the absence of any credible alternative, the most likely explanation is that these cases are linked to exposure to BSE before the bovine offal ban in 1989. This is a cause for great concern."*

This announcement instantly ratcheted-up the British public's concern over the presence of BSE in cattle, and it seems clear that we have not yet heard the last of this concern—a full page

article in the New York Times last Sunday on what happens to the parts of cows that are not eaten by humans seems predictive that the public will express more and more concern.

It seems necessary to start with a bit of background so as to better understand the announcement made in the UK on March 20. [If I had time, I would touch on many points, from the causative agent of BSE, to subjects such as pathology, epidemiology, veterinary clinical medicine, public health, economics, political science, international trade (the European Union, the World Trade Organization), and global governance.] Let me just touch on some key points:

1. First, there is a need to appreciate the nature of prions, the infectious agents that cause the spongiform encephalopathies, that is, scrapie in sheep, BSE in cattle, and Creutzfeldt-Jakob disease (CJD) in humans. Prions are the most bizarre infectious agents ever -- they are "infectious proteins"—"rogue proteins." They have no DNA or RNA like microbes or viruses. Instead, a normal protein that is a constitutive part of the host species is converted to a rogue protein just by contact of a normal molecule with a rogue molecule which has entered the body. Incredibly, the difference between normal and rogue protein is just in the folding of the molecule. As more contact between normal and rogue protein molecules occurs, more and more protein is abnormally refolded. The rogue protein is extremely tough, resisting normal breakdown processes within the body and resisting the means that we usually use to kill viruses and bacteria. Prion proteins resist boiling, resist high doses of γ-irradiation, can even be stored in formaldehyde. The rogue proteins build up in neurons and cause severe brain dysfunction and eventually death. In the past few months there have been new clues about how this damage occurs, but I will not go into that today. The point is that tissue (especially brain tissue) of an animal or human dying of a spongiform encephalopathy is full of very tough rogue protein which is infectious.
2. Scrapie, the sheep prion disease, had been known to be present in the UK for more than 200 years, and offal from scrapie-infected sheep had been rendered into cattle feed for many years. In the late '70s the rendering process was changed, leaving out a solvent extraction step, which in hindsight has been recognized as a key step in inactivating prions. It has been hypothesized, but not scientifically explained, that the scrapie prion present in cattle feed initiated the formation of the BSE prion, and that this "species jump," led to the BSE epidemic in cattle.
3. BSE was first recognized in the UK in 1986. As cattle sickened and died their carcasses were rendered and fed back to more cattle, thereby amplifying the epidemic. A graph describing the epidemic is attached. Cases were also identified in several other countries, as a result of importation of British cattle and feeds-tuffs.
4. By 1988, the Ministry of Agriculture, Foods and Fisheries (MAFF) of the UK issued a prohibition against feeding rendered products derived from cattle back to cattle, but this was not enforced until 1991-1992 (there have been many recent press articles noting continuing scofflaws). In 1989, many countries outside the European Union (EU), including the US, prohibited importation of cattle and materials containing bovine materials from the UK.



New Cases of BSE, United Kingdom (by quarter, 1986 - 1996)

5. By March of this year, 161,663 bovine cases of BSE had been confirmed in the UK, involving 59% of dairy herds (over 33,000 herds) and 14% of beef herds. At the peak of the epidemic in 1993, more than 1,000 cases were reported per week.

6. From very early on in the epidemic questions were asked about human health risk. In 1988, an expert committee was formed in the UK, the Southwood Committee. In 1989: the committee reported: *"...it is most unlikely that BSE will have implications for human health..."* However, in 1990 the British Ministry of Health established a CJD Surveillance Unit. By 1990, the front pages of British newspapers were filled with BSE articles, many begging the question, *"...does BSE pose a risk to human health?"* British government officials responded*"...there is nothing to worry about..."* This of course led the public to become more skeptical. The editors of the distinguished British scientific journal *NATURE* reacted: *"...Never say there is no danger [risk]. Instead, say that there is always a danger [risk], and that the problem is to calculate what it is... Never say that the risk is negligible unless you are sure that your listeners share your own philosophy of life..."* I think this quote sums up the essence of public health practice.

7. On March 20 of this year the British government announced the finding of 10 human cases of CJD that were unusual in several ways (detailed in the April 5th issue of *The Lancet*). Eight of the patients had died(2 patients, age 18 and 31, were still alive); age at death 19-41 (mean 27) (vs. 63 for average age of CJD cases that occur throughout the world). The course of disease in these people had been longer than usual and the lesions in their brains were different than usual. Most of the patients had psychiatric problems as well the usual signs of weakness and dementia seen in CJD. On April 15, an "identical" case was reported in a young man in France. Further, it has been stated that 10 more human cases, including three from the same small town, are being studied in the UK.

8. On March 22, the European Union announced an embargo on all imports of beef from the UK. In response, the MAFF announced a ban on selling meat from cattle more than 30 months of age, a selective slaughter and incineration policy (slaughter to involve up to

15,000 cattle per week, 700,000 per year, 4.7 million over 6 years), at a cost of about £250 million per year, £10-20 billion overall. The European Union offered to pay 70% of the costs, but the political fallout has been incredible, escalating each week until the elections in the UK last week, which the press evaluated as a signal that the handling of BSE may be the straw that breaks the camel's back in regard to the survival of the Tory government.

9. The response to all this in the US has been quite temperate. At a news conference on March 29, a joint action plan was announced: it was stated that the Center for Veterinary Medicine at FDA would expedite rule-making banning ruminant-to-ruminant feeding, but that this would take about 18 months, and in the meantime the present voluntary ban would stay in place. It was stated that APHIS/USDA would increase surveillance (to date, 2,795 cattle brains have been examined in USDA's surveillance program—all have been negative). It was stated that CSREES/USDA would increase education and that ARS/USDA would "gather more scientific information." Contrast this with the press release from the WHO/OIE meeting dated April 2 -- WHO stated that (1) there is enough evidence to state that the causative agent of the human disease in the UK should be considered a new variant of the agent of CJD (to be called the V-CJD agent or prion); (2) all countries must conduct surveillance (cattle and humans); (3) all countries must adopt compulsory notification of cases (cattle and humans); (4) all countries must ban all ruminant-to-ruminant feeding; and (5) all countries must conduct more training. I have talked to people who were at the WHO meeting—each said he was convinced that the British announcement about the 10 cases of V-CJD was sound and that he concurred with WHO's actions.

10. Rationalization, even denial, has been evident in some quarters all along. For example, in 1990, the UK's MAFF issued a statement that the ban on ruminant feeding would terminate the BSE epidemic by 1995. Very soon thereafter it became clear that this would not happen (presently, 300 cases a week are being reported), but, rationalization continued and softer statements began to appear. In 1995, USDA issued a statement noting that *"the incidence of BSE in animals born after the ban is at a much-reduced rate..."* [note the term "reduced rate," not zero rate"] and *"the ban...has been effective in reducing the risk of infection..."* [note again the term "reducing," not "eliminating"]. As late as two weeks ago, I read in British newspapers (which I've been downloading from the *Internet*) statements from British government officials that *"British beef is safe and can be eaten with confidence. The future...depends on a restoration of public confidence..."* Somehow, the difference here between the report of a disease episode, even if not absolutely proven as to causation, and a crisis in confidence escapes me. This is one of the roots of the issue we are discussing here today.

11. What about the future of the epidemic of BSE in cattle in the UK and its possible spillover into humans? No one can say -- infectious diseases have always been unpredictable. Will the epidemic in cattle in the UK absolutely end with the true enforcement of the ruminant-to-ruminant feeding ban, or will it be found that some other transmission pattern is ongoing in cattle, hidden behind the main feed-borne epidemic? If some cow-to-calf or cow-to-cow transmission is occurring, then how will the epidemic truly be terminated, and how will British public confidence ever be restored? How many more cases of V-CJD in humans will there be? We cannot answer these questions; the best we can do is design policy prudently and on the basis of our best expert opinion, all the time keeping a weather eye on events in the UK.

So this, in my view, is the necessary context in which the issue of ruminant-to-ruminant feeding in our country must be addressed. There is scrapie in sheep, but there is absolutely no evidence

of BSE in cattle in our country. Therefore, our planning must be truly preventive (and must overcome all the problems that always face preventive programs).

How can we make sure BSE never gets started in our country, or even better how can we get rid of scrapie as well? Banning, immediately, by expedited rule-making, all ruminant-to-ruminant feeding would add an additional level of surety to the present voluntary ban, but, in my view, this would be a small additional step. In my view, much more needs to be done.

We must support more targeted research, research that FDA needs, research aimed at the highest priority gaps in our knowledge. In my view, FDA's #1 need is for a rapid antemortem diagnostic test, for animals and humans. Over the past several years, we've heard over-and-over that antemortem tests for BSE and scrapie are "just around the corner," but where are they? We need these tests in the field, now. In my view, FDA's #2 need is for research that would allow carcasses to be rendered into truly safe products, thereby recovering some value and avoiding an environmental nightmare (incineration of carcasses will yield the British people just fly-ash and CO_2 and will require a maximum amount of fuel). This is a matter where the rendering industry must be helped. For example, the Canadian government is about to start supporting the application by a company in Alberta of a pilot process that reduces ruminant offal and carcasses to valuable fertilizer and bone meal that, in my opinion, will be absolutely safe. Why cannot our government help in this way, getting this or some other innovative process into the hands of our rendering industry?

It also seems to me that our national leadership in this area must be better supported. FDA's leadership has a big job to do in inspection, regulation, communication, training and public outreach. I hope you will help FDA install a system for cooperative planning involving all pertinent government agencies as well as universities and other institutions. I hope you will help FDA bring in the leaders of our cattle and sheep industries, and our slaughter, processing and rendering industries, so as to come up with a comprehensive plan that is based upon lessons learned from the epidemic in the UK.

CONGRESS OF THE UNITED STATES
House of Representatives
Committee on Government Reform and Oversight
Subcommittee on Human Resources and Intergovernmental Relations

Hearing: **Role of the Food and Drug Administration in Protecting the US Consumer from Food-borne Diseases**

Date: **May 10, 1996**

Testimony of: **Frederick A. Murphy**
School of Veterinary Medicine
University Of California, Davis
Davis, CA 95616-8734

I am Frederick A. Murphy, Dean of the School of Veterinary Medicine, University of California, Davis. Formerly, I was Director of the National Center for Infectious Diseases, Centers for Disease Control & Prevention, Atlanta. I am a virologist with broad experience in human and animal diseases, and I am an administrator with long experience in federal and academic organizational systems. I am here today because I am concerned about our country's organizational and scientific approaches to the prevention of food-borne diseases.

I don't think I need say much about the scope of the food-borne disease problems facing our country. If the worthiness of the problems were not recognized, we'd not be here today.

Similarly, I don't think I need say much about the fact that the problem is different than it was years ago—today, the problem does not stem from filth in our processing plants; rather, most recent important episodes seem to have stemmed from the presence in foods of newly recognized, newly emergent microbes, diabolically adapting to our "high tech" food industries. The case of *E. coli* 0157:H7 is a case in point; so is *Salmonella enteritis* in eggs, other *Salmonella* in poultry, and bovine spongiform encephalopathy (BSE, "mad cow disease") in cattle in the United Kingdom.

Just as with everything else in our lives, these kinds of problems seem to keep getting more complicated. We cannot continue to base our regulatory systems on concepts that were designed years ago. We need "high-tech" systems to deal with "high tech" problems. We need "high-tech" organizational systems to drive necessary changes, and to make sure that these changes are cost-effective.

I think that the resolution of today's food-borne disease problems must come from a new federal organizational paradigm. Because of the specific concerns of this Subcommittee, I will lay out my ideas in a series of increasingly larger umbrellas of coverage. But, first, I should say that my ideas are based upon a few fundamental principles:

First, *form must follow function*, and all of the parts contributing to a function must be integrated. It is the success of the whole that is the key to success, and the key to cost-containment. Integration, in my view, means that the scientific base for food-borne disease prevention must be attached to the regulatory programs—this is the only way that evidence-based decisions and policies can be practicable.

Second, there must be no *duplication of authority or responsibility or effort*. Duplication is the basis for building walls between smaller and smaller units, and this leads to turf wars and cost spirals.

Third, *all decisions and policies must be made with a clear understanding of who is the customer, the constituent.* In my view, the public health sector of the federal government has as its only constituent the consumer, the public itself. In contrast, in my view, the various parts of the agricultural sector have as their constituents a complex mix of producers, processors, shippers, wholesalers, retailers, food service industries (and their trade organizations), as well as the consumer. There is always a bit of a blur caused by this overlap of constituents when specific issues are discussed in the "ag" sector. This is not just a matter involving the agencies of the USDA. In the case in point here today, the FDA's Center for Veterinary Medicine, although a part of the public health sector with its sole responsibility to the consumer, also has had to accommodate the wishes of certain "ag" industries. As I think of organizational paradigms for the future, I see a need for removing this blur, while at the same time accommodating national needs, such as those represented by the realities of commercial food production, international trade standards, and efficiency in government.

Fourth, and last: in my view, *there is an excellent model for an organizational structure for food-borne disease prevention in our country—it may be seen in the overall structural design of the US Public Health Service.* That is, we have three units functionally tied together, each with responsibility for a major area, each linked to the others according to the issue at hand: (1) *NIH is the research unit* with links to the large academic research enterprise of our country and the world; (2) *CDC is the prevention unit* with laboratory and field investigation and surveillance programs and with links to state and local public health agencies; and (3) *FDA is the regulatory unit* with links to state and local regulatory agencies and to experimental medicine and clinical medicine. All three have appropriate links to their single constituency, the consumer, the public at large. Would a version of this organization be helpful for envisioning an optimal food-borne disease prevention organizational system for our country?

So, here is my series of increasingly larger umbrellas of coverage—as they get bigger they keep getting better; but, given the history of the institutions involved, the entrenchment of their interests and the turf issues involved they also get more-and-more difficult to place into practice:

Umbrella 1: A New Organizational Unit Within the FDA

The FDA Center for Veterinary Medicine and certain other units of the Center for Food Safety and Applied Nutrition could be organized into an integrated unit with a holistic mission of using investigational and regulatory approaches to deal with all food-borne disease problems. This organizational idea is based upon the concept that food safety issues of the day cannot be easily compartmentalized. The holistic objective is safe food, not just microbe-free livestock feed, antibiotic residue-free bulk milk or hormone-free meat. The question of the safety to humans of ruminant feed supplements derived from ruminant offal, and the lessons from the BSE episode in the United Kingdom, is not an insular matter. The question of the safety to humans of animal feeds containing *Salmonella* is not an insular matter. These examples should remind us of how little research data we have in hand, and how little systems research is going on. Every issue concerning food safety reflects a continuum of risk and risk prevention that extends throughout the "high tech" food chain, from the farm to the restaurant and kitchen. Solutions to specific problems require dealing with specific parts of the food chain, some parts now falling under the auspices of the FDA's Center for Veterinary Medicine, some under other units of FDA's Center for Food Safety and Applied Nutrition, some under agencies of the USDA and the Department of Commerce (seafood safety). Yet others fall through cracks in the federal system and land in state and local health and "ag" agencies. Integration would force many progressive changes.

Umbrella 2: A New Organizational Unit Within the Public Health Service

Following the same logic, FDA's Center for Veterinary Medicine, certain other units of FDA's Center for Food Safety and Applied Nutrition, certain units of the CDC (National Center for Infectious Diseases) and perhaps certain units of the NIH could be organized into an integrated unit with an even more holistic mission. This Public Health Service-based unit could carry out the investigational and regulatory missions already mentioned, and could also integrate the powerful elements of surveillance, modern

diagnostics, and research. This unit could employ present links to state health department surveillance and diagnostics systems and could, via NIH's extramural research system, bring the research horsepower of academic medicine, veterinary medicine, public health and biomedicine to bear on food-borne disease problems. The more I think of this umbrella idea, the better it seems.

Umbrella 3: A New Organizational Unit Within the US Government

Going further, the same logic could be extended from this Public Health Service-based organizational unit to encompass all aspects of federal food safety responsibilities. This would require melding of authorities now held in several agencies of the USDA and the Department of Commerce, along with all the Public Health Service units already mentioned and perhaps a few others (DOD?, EPA?). This would require the formation of an agency, the "Food Safety Agency." This agency, designed from scratch, could best lead to a rebalancing of all federal food safety programs toward the right mix of applied research, surveillance, diagnostics, inspection (monitoring) and regulatory activities needed in this "high tech" era. This agency could be organized along the lines of the Public Health Service, overall, with a research unit(supporting intramural and extramural applied research to fill in crucial gaps in our knowledge), a surveillance unit (with field unvestigation capabilities) and an inspection and regulatory unit (with ties to state and local food safety agencies) (inspection regulatory activities must always be kept separate since relationships between government and prive sectors are different here). In my view, this new "Food Safety Agency" could best represent the needs of the consumer, while at the same time it could deal with the needs of producers in this expanding, globalized economy. As I think about this third umbrella idea, I become even more upbeat.

How could these umbrella ideas, especially the third one, be explored? One idea comes to mind: would this Subcommittee consider charging an independent organization, such as the National Research Council/National Academy of Sciences with developing a national strategic plan of this sort? If this were done, we might have a consensus strategic plan in place in a year or so.

Thank you.

ATTACHMENT:

For the record, I am attaching the following document which provides more background and rationale for the proposals made above.

1. The Forces for Change in Assuring Food Safety

There is a rising tide of public expectation that our food be made safer than it is today. Part of this expectation follows upon a false sense of danger—in fact, we have the safest food supply in history. On the other hand, part of this expectation stems from media coverage of real episodes which suggest that we could do better, and from statistics which suggest the same: for example, CDC estimates that there are more than 80 million cases of food-borne disease in the United States each year, with over 9,000 deaths and more than $1 billion in costs. National surveillance data show that microbial contamination is by far the most important contributor to these data, yet the public is also concerned with the more mysterious risk of chemical contamination (pesticides, herbicides, antibiotic residues, etc.). That is, the public easily extends its concern from the Alar/apple episode to the *E. coli* 0157:H7/hamburger episode. The public also perceives that changes in farming and processing industries have created new situations where microbial pathogens can be introduced into foods, whether at the source on the farm, or in the many steps in processing and distribution. In this regard, the media has featured many different problems, some pertinent to poultry, some to seafood, some to beef and pork, some to vegetables and fruit, and some to the food distribution, retailing and restaurant systems, per se. The positive side of this is that the public is very supportive of programs that will make our food safer.

2. The Complexity of the Food Chain in Regard to Food Safety

The food chain is becoming extremely complex and changing in many ways: (1) food production and processing units are becoming larger, turning out larger lots of products (so when something goes wrong there are greater consequences and there is greater public notice); (2) there is increasing diversity of products—approximately 2,000 new food products reach the market each year (most are quite technically intricate and many contain untested ingredients, additives, and involve unusual processing steps); (3) there is increasing public demand for "ready to eat" processed foods (this involves large numbers of food handlers, extended holding of products at room temperature, and increasing opportunities for microbial contamination and amplification); and (4) there is increasing demand for ethnic food products (some of which may not be prepared to conventional safety standards). For these and many other reasons, our country's food safety system must be streamlined, and recast with a sounder scientific basis. We need a system based on *"assessment of the process, not the product."* We need a system that is *preventive* in that it identifies places in the food production and processing chain where problems are most likely to occur and focuses inspection and regulatory actions at these points. Further, we need a system that focuses applied research, surveillance and field investigations at these same points.

The modern food chain has been characterized as "preharvest" for all aspects of production up to the processing plant and "postharvest" for everything occurring from the processing plant to the table. Preharvest factors that have increased the potential for food contamination include larger production units, specialized production practices such as monocultures (uniform groups of animals, as is the case in the poultry industry) or stratified animal raising. The concentration of animals in larger production units has both benefits and risks. The benefits include economies of scale, a more uniform product and better sanitation. The risks includes potential for significant losses because of disease. The disease threat tends to require more intense management schemes. As a result, management often resorts to the use of chemicals or antibiotics as preventive measures to assure ongoing production.

Contamination can be easily spread through large quantities of foods in postharvest handling systems mainly because of mixing of products from many sources and distribution of food products widely, often across state lines. Contamination of carcasses may occur in processing plants if equipment and utensils are not properly handled and strictly sanitized; further contamination may occur as foods are processed by wholesalers. In the end, contamination from a single source can result in the infection of very large numbers of people: in the case of the 1993-94 episode in the Northwest where hamburgers were contaminated with *E. coli* 0157:H7, many thousands of patties became contaminated, and many thousands of people were at risk. Recently, very large lots of cantaloupe, lettuce and tomatoes have been contaminated with Salmonellae and other agents. Water used to clean vegetables can easily become contaminated resulting in whole lots becoming contaminated.

3. Microbial Factors Affecting the Emergence of Food-borne Diseases

The emergence of over thirty new causes and sources of food-borne diseases in the last 25 years suggest the importance of continuing efforts in research, diagnostics, and agent-specific surveillance. The emergence of new microbial food-borne threats is best exemplified by *E. coli* 0157:H7 infections which were first recognized in 1982. Between 1982 and 1992, there were 17 reported outbreaks; but in 1993 there were 17 and in 1994 there were 25 major outbreaks throughout the United States. Microbial contamination resulting in serious food-borne diseases has been associated with melons, tomatoes, asparagus, apples, potatoes, mushrooms, lettuce, eggs, meat, dairy products and seafood, among other foods. Microorganisms undergo genetic changes or acquire transposable genetic factors, that is "virulence" factors. These adaptive changes may be associated with the emergence of new microbial strains such as *E. coli* 0157:H7 which cause severe disease, especially in children. The misuse of antibiotics has led to antibiotic drug resistant strains of bacteria that are difficult to treat and, as a consequence can overwhelm the patient and cause death. The continuing emergence of food-borne diseases is a clear indication of the need to re-examine the factors that are contributing to these infections at all steps in the food chain.

4. The Immune Status of the Population and the Presence of Persons at Risk of Severe Disease

Public health officials are increasingly concerned about the growing potential for food-borne diseases caused by infectious agents in people with compromised immune systems. This includes the very young, the aged, the poor, and individuals with AIDS, cancer, diabetes, and other debilitating diseases. The increase in the environment of chemical residues, some of which are immunosuppressive, also impacts the population. These factors will increase susceptibility to food-borne diseases, leading to more cases of severe disease and even death. Food-borne diseases cause more than diarrhea; the after-effects of a food-borne disease episode may be complicated by chronic diseases such as arthritis, heart and vascular diseases, renal failure, hemorrhagic syndromes, stroke, abortion, chronic malabsorption syndromes, and malnutrition.

5. Societal Changes and Food Safety

One consumer concern arises from the fact that no agency is really responsible for the safety of the diversity of food products that we see in the supermarket. With many different individuals producing food products, many intermediate food handlers involved in processing, distributing, wholesaling, retailing and preparing foods, responsibility for food safety is distributed so widely that no one seems to be responsible for product safety. The increasing globalization of the food supply and the role of the North American Free Trade Agreement (NAFTA) and the World Trade Organization (WTO) complicate this matter greatly. These trade agreements mean that our food supply will require greater monitoring and management than has been the case in the past. Within the US food industry, the opportunity for major outbreaks of food-borne diseases will increase because the risk of contaminating very large lots of food products. For example, a Salmonellosis outbreak stemming from a problem in an Illinois dairy plant in 1985 affected over 197,000 people, causing hundreds of hospitalizations and many severe disease episodes. In addition, the distribution of single source foods to schools, hospitals, and nursing homes tends to cluster the number of cases involved in large outbreaks that can overwhelm local health care facilities and local public health agencies.

6. The Economic Impact of Our National Food Safety System

The economic impact of food-borne diseases affects society in many ways: (1) causing lost productivity and increased health costs and (2) causing the loss of food product sales and commensurate economic disruption. Food-borne diseases and contaminated food products are also serious causes of economic disruption at the local, national and international levels. The 1993-94 outbreak of *E. coli* 0157:H7 from a fast food restaurant chain in Northwestern United States resulted in incredible health care costs—some patients were still under medical care two years after their initial disease. The overall economic loss from missed work and decreased work efficiency is estimated at $30 billion annually in our country. The major concern is not just lost income. The loss of consumer confidence in food products that have been identified as being contaminated with microbial agents can cause dramatic shifts in consumer purchasing habits, often leaving a surplus of perishable items that have to be discarded at great economic loss to producers, processors, wholesaler and retailers.

7. Research: Identifying Gaps in Our Knowledge

The current food safety system needs to be modernized by redirecting food safety activities and emphasizing human health concerns, per se. This requires a better assessment of the causes of food-borne diseases. We must learn which steps in our food chain system contribute to particular diseases. We must learn what actions must be taken to correct each risk situation. Included in this is a better coordinated public health surveillance system for detecting and reporting human disease and a coordinated effort by all parties to monitor and eliminate risk situations. Systems approaches, such as Total Quality Management (TQM), ISO 9000, and Hazard Analysis Critical Control Point (HACCP) are the key, and must be applied from preharvest to postharvest elements in the food chain. Models of these systems need to be developed—we need a new research paradigm to do this. Risk assessment must

form the basis for risk management, the policy aspect of risk assessment. Models can then be developed and used for teaching and demonstrating the appropriate ways to handle foods throughout the food chain.

8. Education and Training in Food Safety

There is a critical need to provide better ways for educating food handlers. The challenge includes a better understanding of scientific and hygienic principles, addressing the illiterate or non-English speaking immigrants that are often hired as food handlers or as farm laborers and informing the general public about risks with food preparation. The responsibility of food safety is a shared responsibility involving every individual that participates in producing or handling food, including employers. Failure to effectively inform, monitor and assure safe handling of food will be subject to litigation. Educating food handlers will require major efforts, but the benefits will be enormous.

New curricula need to be developed that emphasize food safety and the impact of food-borne diseases in preharvest and postharvest settings. There is an increasing need for leaders and mid-level professionals who understand the broad scope of food safety as it must be practiced in today's complex food industries. This requires more people trained in public health, veterinary public health, epidemiology, food microbiology, extension and outreach in the work force to assist in effecting change.

9. The Need for Cooperation at the Interface Between Agriculture and Public Health

In the past, it was assumed that the agricultural sector would be responsible for assuring that our food supply is safe. The regulatory agencies of the USDA and state governments were empowered by long-standing laws and public funds. However, in the past few years, as the forces for change have been developing, and as the Congress has debated food safety, the otherwise quiet responsibilities of the public health sector for certain aspects of food safety have become better known. At the same time, the public health agencies, at the federal and state levels, have been extending their activities into more and more of the newer food safety issues and episodes: the public health sector took the lead in the *E. coli* 0157:H7 hamburger episodes, *Salmonella enteriditis* egg episodes and *Listeria* in cheese episodes. This has led to tensions, which have been exacerbated as it has been suggested that we need a single encompassing new federal agency, the "Food Safety Agency," involving units of the FDA, the Public Health Service, the Department of Commerce (seafood safety), and the USDA. This kind of turf battle may just be a reflection of the public's sense that something better is needed—in many discussions of this subject is an expressed wish that the interface between agriculture and public health sectors be improved. Any success in advancing our national food safety agenda will depend largely on making this interface a smooth base for cooperation and collaboration, not a "line in the sand" for turf arguments. A smooth interface will serve common research, educational and program activities. Since the academic sector, that is, academic agriculture, veterinary medicine, medicine and public health, are all involved, it goes without saying that a smooth interface is needed here too.

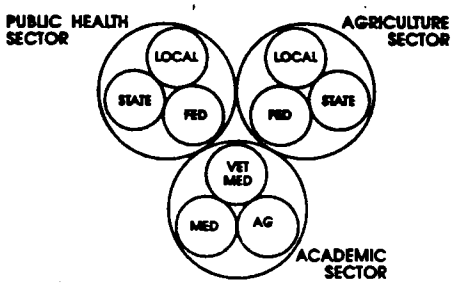
10. An Action Plan for a New Food Safety System for Our Country

The underpinnings for an action plan for a new organizational paradigm for food safety activities in the federal government is presented at the beginning of this document. It is presented as a series of increasingly large umbrellas, leading in the end to an idea for a new federal agency, the "Food Safety Agency," that would have responsibility for all food safety activities at the national level, and would have responsibility for bringing together holistically all state, local and academic interests that are meant to serve the same needs.

Several characteristics of our national food safety enterprise must be recognized in fattening out this idea: (1) there are many different people involved, many different responsibilities and interests represented; (2) because of the number of people and agencies involved and the diversity of their responsibilities and interests, there is need for increased communication, cooperation and collaboration (the *three Cs*); (3) the responsibilities and interests of all the people and agencies involved do not overlap too much, therefore the assemblage of working level units into a new overall organizational system need

not be the cause of endless turf battles; (4) the interests of the public must be paramount and interdigitated into all the professional responsibilities and interests of concerned professionals; and (5) leadership is the key to the success of the enterprise and leaders must employ systems that provide flexibility and simplicity for the running of the new enterprise

For example, here is one view of the potentially involved units, by categories, not by individual interests. At the hub of this diagram would be the new federal Food Safety Agency.



Consider how the different players might work together under different circumstances. For example, consider a food-borne disease problem, serious in nature, statewide in distribution, but not requiring much new research or development—consider a hepatitis A outbreak traced to a food service vendor. state and local public sector agencies would work together, but it might not be necessary to draw in federal agencies or academic or agriculture sectors. But, just as soon as a working relationship like this might be set in place, consider the possibility that another issue could emerge which might involve, additionally, state and local agriculture agencies—perhaps the hepatitis A outbreak is traced to a food manufacturer, not just a food service vendor. Or, consider the possibility that state and local health departments might face a somewhat different problem, such as a mysterious unusual hepatitis outbreak, not hepatitis A, perhaps with some food-based linkage. This might grow into a problem that cannot be resolved immediately, a problem calling for epidemiologic field study, a problem that might be cracked only by research requiring the combined efforts of several Schools of Medicine, Schools of Veterinary Medicine, as well as the new "Food Safety Agency." Clearly, great flexibility is called for—the overall interests of a safe food supply are served by a strong central leadership agency, with broad authority and responsibility, an agency that would be expected to leverage its resources from the diverse pool of talent and interests represented by state, local and academic participants.

How might such a flexible enterprise be organized? One idea, or the seed of an idea, is represented in the proposal made at the beginning of this document. Would this Subcommittee of the Congress consider charging an independent organization, such as the National Research Council/National Academy of Sciences, with developing a national strategic plan toward this end?

One would hope that the resulting strategic plan might guide our country in developing: (1) a system for central national leadership in food safety; (2) a system for research, education and training; (3) a system for assuring solid public policy; (4) a system to draw in food producers, shippers, and providers, as well as professionals in fields such as public health, veterinary medicine, epidemiology, microbiology, and extension/outreach; (5) a system for food safety assurance, based upon HACCP, risk assessment, TQM, and other proven approaches; (6) a system to assess economic and environmental impacts of actions; and (7) a system to assure a realistic funding base for meeting these societal needs. All this could start with strategic planning for a new federal "Food Safety Agency."

This Attachment was prepared by my colleague, Dr. Bennie I. Osburn and myself. It does not reflect the positions of others representing the University of California, the Association of American Veterinary Medical Colleges (AAVMC) or the National Association of State Universities and Land Grant Colleges (NASULGC), all of whom have positions on the subject at hand.

Mr. SHAYS. What would be your bottom line two points to this committee?

Dr. MURPHY. That a ban on ruminant-to-ruminant rendered product is reasonable. And if it's going to be done, that the tradition of the FDA, to err on the side of safety, argues that we do it now. And that research is urgently needed to give FDA tools to prevent any further problems. Thank you.

Mr. SHAYS. Thank you very much. Dr. Crawford, I've been pretty lenient with the 5-minute rule in part because I did interrupt you. But I'm going to try to stick a little closer to the 5-minute rule. I'll let you go over it a little bit.

Mr. CRAWFORD. Thank you very much. I'm a veterinarian who serves as executive director of the Association of American Veterinary Medical Colleges. Our association is the primary coordinator of the affairs of North American veterinary colleges, departments of veterinary science, departments of comparative medicine, and animal medical education centers. Our member institutions are dedicated to improving animal and human life, addressing the interests of animals as well as those of pet owners, livestock and poultry producers, and consumers of food and fiber derived from animals.

I was for 5 years through 1985 Director of FDA's Center for Veterinary Medicine. After a brief stint at the World Health Organization, I served from 1987 to 1991 as Administrator of the Food Safety and Inspection Service of USDA. I am pleased to respond, Mr. Chairman, to your request to focus on FDA's regulatory review of animal feeds that have an impact on the safety of the food supply, including ruminant-to-ruminant feeding practices.

The first principle, I believe, to consider is that animal feeds represent not just a source of concentrated nutrition, but a dosage form for medications both to prevent and to treat disease conditions. The approval process for feed additives must be as rigorous and thorough as for other dosage forms, including injectable and traditional oral medications.

Two of this Nation's most serious animal chemical residue incidents occurred as a result of feed contamination. In 1975 and 1976, thousands of cattle in Michigan had to be destroyed because polybrominated biphenyls or PBB's were inadvertently mixed in dairy cattle feed rather than in bags intended for use as a fire retardant. In the late 1970's, sulfamethazine residues in swine affected more than 5 percent of the U.S. herd. Other incidents involving various other substances have plagued America's livestock producers off and on until comparatively recent times.

The examples that I gave were aberrant and have never been repeated, but they do point out the need for regulation and also for self-compliance by the industry.

FDA and certain professional and trade organizations are seeking to create a mechanism whereby veterinarians could exercise more oversight over feed additives. I strongly support that mechanism which is being called the veterinary feed directive. The VFD, or veterinary feed directive, initiative would create by risk assessment a class of feed additives that would require a veterinarian's order before usage. Under this scheme, when a non-over-the-counter drug needed to be added to feed, a food producer would

consult with his or her veterinarian to determine exactly which product should be ordered, at what dosage level, and how frequently it should be administered.

The food producer would then present the ensuing VFD to the feed milling company where the medication would be added to the feed in accordance with the veterinarian's directions. All parties involved would be required to keep careful records. Implementation of the VFD would provide, in my view, a necessary extra safeguard and perhaps encourage a more expeditious approval process for feed additives of special promise. The approval process for feed additives, as well as for other veterinary drugs, should be streamlined in my view because experience has shown that each new generation of animal drugs are, in general, safer and more effective.

This is something that you're obviously very familiar with. It's been brought up earlier in the first panel. It's in House bill 3200, the Drug Availability Act. And I congratulate both you and Mr. Towns on your foresight of this direction. And I do hope it passes.

On the question of ruminant-to-ruminant feeding, the World Health Organization [WHO] addressed this issue at the expert consultation held in Geneva, April 3, 1996. They observed that the current BSE epidemic in the United Kingdom appears to have been transmitted to cattle via contaminated meat and bone meal in concentrate feed, with sheep or cattle being the original source. Although BSE now occurs in other countries, not including the United States, the United Kingdom's disastrously high incidence was thought by WHO to have been due to the recycling of affected bovine material back to cattle.

Although the BSE epidemic continues in the United Kingdom with new cases confirmed each week, the number of cases has declined appreciably since the banning of ruminant-to-ruminant feeding in 1988. Finally, WHO recommended that all countries ban the use of ruminant tissues and ruminant feed whether or not BSE is present in such countries.

It should be noted that a number of organizations, including my own, have called for a voluntary ban on ruminant-to-ruminant feeding while FDA studies the situation. It also should be noted that FDA issued a proposed regulation in 1994 that would ban the use of sheep and goat, but not cattle, offal in animal feed. And it could be that FDA's dilemma has been answered today by the issuance of an advance notice of proposed rulemaking wherein they would seek information on whether or not to include all ruminants in that ban.

FDA regulations, as you well know, must meet a rigorous scientific as well as legal standard. And I think their initiative to request more information is probably the proper course, given the constraints they're given and have to operate under. However, I must say that the World Health Organization consultation seems to me to have removed much of the uncertainty. This was an expert consultation. They said until more is known, ban ruminant-to-ruminant feeding. And that's something that sounds reasonable indeed to me.

Thank you, Mr. Chairman, for the privilege of being here today. I would be pleased to respond to comments and questions.

[The prepared statement of Dr. Crawford follows:]

Dr. Lester M. Crawford, DVM, PhD
Executive Director
Association of American Veterinary Medical Colleges

Thank you very much, Mr. Chairman, for the opportunity to present my views before this committee. I have a five minute summary, but would like to reserve the right to provide additional information.

I am a veterinarian who serves as Executive Director of the Association of American Veterinary Medical Colleges (AAVMC). AAVMC is the primary coordinator of the affairs of North American veterinary medical colleges, departments of veterinary science, departments of comparative medicine and animal medical education centers. Our 51 member institutions are dedicated to improving animal and human life by addressing the interests of animals as well as those of pet owners, livestock and poultry producers and consumers of food and fiber derived from animals.

I was for five years (through 1985) Director of FDA's Center for Veterinary Medicine. After a brief stint at the World Health Organization in Geneva, I served from 1987-91 as Administrator of the Food Safety and Inspection Service of USDA. I am pleased to respond to your request to focus on FDA-CVM's regulatory review of animal feeds that have an impact on the safety of the food supply, including ruminant-to-ruminant feeding practices.

The first principle to consider is that animal feeds represent not just a source of concentrated nutrition, but a dosage form for medications both to prevent and to treat disease conditions. The approval process for feed additives must be as rigorous and thorough as for other dosage forms including injectable and traditional oral medications.

Two of this nation's most serious animal chemical residue incidents occurred as a result of feed contamination. When I was first at FDA in 1975-76, thousands of

cattle in Michigan had to be destroyed because polybrominated biphenyls (PBBs), a fire retardant, were inadvertently mixed in dairy cattle feed. In the late 1970s, sulfamethazine residues in swine affected more than 5 percent of the US herd. Other incidents involving various other substances have plagued America's livestock producers off and on until comparatively recent times.

FDA and certain professional and trade organizations are seeking to create a mechanism whereby veterinarians could exercise more oversight over feed additives. I strongly support that mechanism which is being called the veterinary feed directive (VFD). The VFD initiative would create, by risk assessment, a class of feed additives that would require a veterinarian's order before usage. Under this scheme, when a non over-the-counter drug needed to be added to feed, a food producer would consult with his or her veterinarian to determine exactly which product should be ordered at what dosage level and how frequently it should be administered. The food producer would then present the ensuing VFD to the feed milling company where the medication would be added to the feed in accordance with the veterinarian's directions. All parties involved would be required to keep careful records. Implementation of the VFD would provide, in my view, a necessary extra safeguard and perhaps encourage a more expeditious approval process for feed additives of special promise. The approval process for feed additives as well as for other veterinary drugs, should be streamlined because experience has shown that each new generation of animal drugs are in general safer and more effective.

On the question of ruminant-to-ruminant feeding, the World Health Organization (WHO) addressed this issue at the expert consultation held in Geneva, April 2-3, 1996. They observed that the current bovine spongiform encephalopathy (BSE) epidemic in the United Kingdom appears to have been transmitted to cattle via

contaminated meat and bone meal in concentrate feed, with sheep or cattle being the original source. Although BSE now occurs in other countries, not including the US, the UK's disastrously high incidence was thought by WHO to have been due to the recycling of affected bovine material back to cattle. Although the BSE epidemic continues in the UK with new cases confirmed each week, the number of cases has declined appreciably since the banning of ruminant-to ruminant feeding in 1988. Finally, WHO recommended that all countries ban the use of ruminant tissues in ruminant feed whether or not BSE is present in such countries.

It should be noted that the National Cattlemen's Beef Association, American Sheep Industry Association, National Milk Producers Federation, American Veterinary Medical Association, Association of American Veterinary Medical Colleges, and American Association of Bovine Practitioners all have called for a voluntary ban on ruminant-to-ruminant feeding while FDA studies the situation. It also should be noted that FDA-CVM issued a proposed regulation in 1994 that would ban the use of sheep and goat, but not cattle, offal in animal feed. It could be that FDA's dilemma is based on whether or not to include cattle tissues in the ban. If so, their reticence may be based on the adequacy of the science. FDA regulations must meet a rigorous scientific, as well as legal, standard.

Thank you Mr. Chairman for the privilege of being here today. I would be pleased to respond to comments and questions.

Mr. SHAYS. I thank the gentleman. I just want to say that I'm impressed with the panel that we have before us and your backgrounds. And it's nice that you all made the time to come here today. I really appreciate it. Dr. Weber.

Mr. WEBER. Thank you, Congressman. My name is Gary Weber. I am representing the National Cattlemen's Beef Association. I have a B.S. and M.S. degree from Purdue University in animal science. And when Congressman Souder was here, my home farm is in his district. He's not here right now, but I thought I'd mention that.

Mr. SHAYS. I'll make sure that he'll know he missed you.

Mr. WEBER. I was glad to see him today. I have a Ph.D. from Michigan State University also in animal science. I worked for over 10 years for the U.S. Department of Agriculture, the last of which I served as a national program leader for animal science for the USDA Extension Service.

For the last 2 years and in my current capacity, I worked in the area of legislative and regulatory efforts to ensure the health and well-being of cattle and to enhance the safety, wholesomeness, and affordability of our products for consumers. The National Cattlemen's Beef Association is very pleased to be provided this opportunity to testify before the subcommittee.

Let me preface my other remarks by indicating the scope and impact of the beef cattle industry in the United States. We represent the largest segment of agriculture. The total retail value of beef produced in 1985 exceeded $50 billion. The sale of cattle and calves ranges from $35 to $40 billion annually and accounts for more than 20 percent of all agricultural marketings from the farms and ranches.

When the meat processing sector is included, the total number of jobs in the United States associated with the beef industry exceeds 1,560,000. And this other side of the industry provides $68 billion of personal income.

Mr. SHAYS. Is that the total amount?

Mr. WEBER. If you add all of those up, it's about $153 billion business in the United States, from farm to table.

The beef industry also contributes to a reduction in the U.S. trade deficit. We are the world's largest exporter of beef. And our exports now exceed for the first time this year our imports.

The National Cattlemen's Beef Association and the producers that we represent take any threat to the health and well-being of our cattle seriously. We are especially concerned when there is a potential for an illness in cattle that could even remotely affect consumers or even the perception of consumers about our products. We have a reputation around the world for having the most healthy cattle and the safest, most wholesome and high quality beef in the world. We work diligently to protect the health of our cattle, the safety and wholesomeness of our products and our reputation here and around the world.

As a result of this commitment, we have aggressively supported Government actions dating back to 1985 to keep the disease identified in Great Britain as bovine spongiform encephalopathy or BSE out of the United States. And we have been impressed with the way the Government has acted since 1985 to protect our cattle pop-

ulation from this disease, and that the rendering industry and the sheep industry in 1991 put in place a very effective voluntary ban on the use of sheep in the rendered material. And I think that should have been mentioned earlier in the other panel, that that has been very effective in further reducing the risk to the cattle population.

But for us, it is clear that, as we look at the epidemiology studies, that BSE being a unique disease in Great Britain of unknown origin causes us concern. We have to clarify that it's not caused simply by feeding ruminant derived protein back to ruminants. But if you have the disease in cattle, this mode of feeding would spread it. And there is scientific evidence that indicates there are specific processing steps which can inactivate these disease causing agents. So it's conceivable that the transmission of these diseases through ruminant derived proteins could be eliminated if we have these steps taken within the system.

Given this and other information, on March 29, 1996, the National Cattlemen's Beef Association announced that we would ask all beef and dairy producers and the feed industry to cease incorporating ruminant derived proteins in the diets for beef and dairy cattle. We request that this action be taken until the Food and Drug Administration, Center for Veterinary Medicine has completed the type of comprehensive review of the scientific literature that they are proposing today.

Our decision is based on our intent first and foremost, to protect the health of the U.S. cattle herd and eliminate any risk, no matter how remote of a public health threat. And I have to emphasize that since we do not have BSE in the United States, as documented by 10 years of monitoring surveillance and action, this additional step will totally—and prefacing Dr. Murphy's comments, we want to be careful to say no risk—but it virtually eliminates the risk of BSE occurring in this country by the steps we've taken and these additional measures.

Our decision is supported, as Dr. Crawford has said, by a number of organizations and professional organizations and the WHO. But obviously we must base our decisions on science. Our actions have been taken because we feel the science indicated prevention of BSE must be our highest priority. If, after a comprehensive review of the scientific evidence, the Food and Drug Administration, Center for Veterinary Medicine, can identify the specific processing steps necessary to inactivate the BSE agent or other TSE agents, we may be able to reconsider our voluntary ban of feeding these proteins.

In any event, since we do not have BSE in the cattle population in the United States, our actions with this ban not only protect our cattle but also maintain the quality and safety of these ruminant derived protein products for other uses.

Thanks again for this chance to discuss this with you.

[The prepared statement of Mr. Weber follows:]

My name is Gary Weber, I am representing the National Cattlemen's Beef Association. I have a B.S. and M.S degree from Purdue University in Animal Science and a Ph.D. from Michigan State University. I worked for over 10 years for the United States Department of Agriculture, the last 7 I served as the National Program Leader for Animal Science for the USDA-Extension Service in Washington, DC. In my current capacity I work in the area of legislative and regulatory efforts to ensure the health and well-being of cattle and enhance the safety, wholesomeness and affordability of our products for consumers. The National Cattlemen's Beef Association is pleased to be provided this opportunity to testify before this subcommittee.

Let me preface my remarks by clarifying the scope and impact of the beef industry in the United States. We represent the largest segment of agriculture. The total retail value of beef produced in 1995 exceeded $50 billion. Sales of cattle and calves, ranging from $35 to $40 billion annually account for more than 20 percent of all agricultural product marketing. When the meat processing sector is included, an estimated 1.56 million jobs and $68.1 billion of personal income are generated by the beef industry.

The beef industry also contributes to a reduction in the U.S. trade deficit. During 1995 beef and beef variety meat export value exceeded $3.25 billion. Exports of cattle, hides and other by-products brought the industry's export total to $5.4 billion, compared to an import total of $3.0 billion.

The National Cattlemen's Beef Association, and the producers we represent, take any threat to the health and well-being of our cattle seriously. We are especially concerned when there is the potential for an illness in cattle to even remotely effect consumers, or even the perception of consumers about our products. We have a reputation around the world for having the most healthy cattle and the safest, most wholesome and high quality beef in the world.

We work diligently to protect the health of our cattle, the safety and wholesomeness of our products, and our reputation here and around the world. As a result of this commitment, we have aggressively supported government actions, dating back to 1985, to keep the disease identified in Great Britain as Bovine Spongiform Encephalopathy or BSE out of the United States.

We have no BSE in the United States and the following steps have been taken to prevent BSE from entering the United States.

We have imported no beef from Great Britain since 1985.

In 1989 APHIS banned the importation of live ruminants and ruminant products from countries where BSE is known to exist.

• In 1986, APHIS established a program for BSE surveillance in the U.S. and provided specialized training for 250 APHIS veterinarians who conduct field investigations involving suspicious symptoms. From 1986 to March, approximately 2,800 brain specimens from cattle exhibiting possible neurological problems in 42 states have been studied by APHIS. All samples submitted have been negative.

• APHIS veterinary pathologists and field investigators have received training from British counterparts for diagnosing BSE.

• Over 60 veterinary diagnostic laboratories throughout the United States are participating in the BSE Surveillance Program (initiated in May 1990) along with the National Veterinary Services Laboratories in Ames, IA.

• APHIS veterinarians have traced the 499 head of cattle imported from Great Britain between 1981 and 1989 (before the ban on imports went into effect) to check their health status. As of April, 1996 less than 90 imports are known to be alive; 341 are known to be dead; and eight imports have been exported. There is an active effort to purchase the remaining cattle imported from Great Britain. None of the remaining animals will enter the feed or human food chain. The animals that are alive are monitored regularly, and no signs of BSE have been found. All animals purchased are being evaluated for any signs of BSE in the laboratory.

• Since 1991, there has been a voluntary ban in place on the use of rendered products from adult sheep in animal feeds.

It is clear from the epidemiology studies that BSE is a unique cattle disease originating in Great Britain. It is a disease of unknown origin. It is not caused by the feeding of ruminant derived proteins back to ruminants. However, if cattle were to acquire the disease, the practice of feeding ruminant derived proteins to cattle could spread the disease. There is also scientific evidence indicating the specific processing steps necessary to inactivate the disease causing agent. If these processing steps are employed, it is conceivable the risk of transmission from ruminant derived proteins could be eliminated.

Given this, and other information on March 29, 1996, the National Cattlemen's Beef Association announced that we would ask all beef and dairy producers, and the feed industry to cease incorporating ruminant derived proteins in the diets for beef and dairy cattle. We request this action be taken until the Food and Drug Administration - Center for Veterinary Medicine has completed a comprehensive review of the scientific literature pertaining to BSE.

The decision is based on our intent to first and foremost protect the health of the U.S. cattle herd and eliminate any risk, no matter how remote, of a threat to public health. Since we do not have BSE in the United States, as documented by 10 years of monitoring and surveillance data, our actions now will totally prevent BSE from ever occurring in the United States.

Our decision is supported by the National Milk Producers Federation and American Sheep Industry Association.

Our actions are endorsed by the American Society of Animal Science, American Association of Veterinary Medical Colleges, American Veterinary Medical Association, and the American Association of Bovine Practitioners.

Our decision is also consistent with the position taken by the World Health Organization (WHO) at a recent meeting in Geneva, Switzerland on April 2-3, 1996.

Obviously, we must base our decisions on science. Our actions have been taken because we feel the science indicated prevention of BSE must be our highest priority. If, after a comprehensive review of the scientific evidence, the FDA-CVM can identify the specific processing steps necessary to inactivate the BSE agent, we may be able to reconsider our voluntary ban on the feeding of these protein products.

In any event, since we do not have BSE in the United States, our actions ensure the safety and quality of ruminant derived protein by-products for other uses.

Mr. SHAYS. Thank you, Dr. Weber. Dr. Franco.

Dr. FRANCO. Mr. Chairman, the subcommittee has my testimony for the record. Twenty-five years of my career was in food safety as an employee of the U.S. Department of Agriculture. Incidentally, my former administrator is right here. We shared many good years in the realm of food safety.

Mr. Chairman, without a doubt, the transmissible spongiform encephalopathies are complex. Up to 8 years ago, some of the Nation's most renowned research neural pathologists have described scrapie, the prototype of the TSE, as slow viruses. Today, Mr. Chairman, we are aware that current knowledge does not support that causative theory.

Unfortunately, more is unknown than known. As a result, our industry strongly recommends that the evaluation of regulatory options by the Food and Drug Administration be based totally on science and not on public perception or political expediency.

You alluded, Mr. Chairman, this morning to the words, sound science, to address this issue. I validate your thinking. Inferences, anecdotes, and presumptive speculation are poor substitutes. If FDA ever deviates from risk-based science, a precedent could be established that we may all ultimately regret. One only needs to review the aftermath of the recent disastrous BSE panic in the United Kingdom to get a graphic example of this point in its extreme.

The cause of the bovine spongiform encephalopathy complex remains unknown. All of the current hypotheses are inferences. There have been broad differences of opinion within the scientific community. There is absolutely nothing that approaches consensus. Debate and dissent remains constant. Research findings tend to contradict and cloud any potential resolution of the issue in the immediate future. There is also absolutely no proven evidence, aside from epidemiological analogies to associate scrapie to BSE or BSE to Creutzfelt-Jakob disease. Thus, a pressing need obviously for continued research is absolute.

We believe a ruminant-to-ruminant feed ban makes sense and is warranted in countries where BSE exists in the present cattle population. Such a policy is prudent and responsible. In countries without any evidence of BSE, however, and in a different risk category, it should be treated differently. Requiring a ruminant-to-ruminant feeding ban for lower risk countries like the United States is not based on current scientific evidence and is premature in our judgment.

The public health inference, Mr. Chairman—without going into any detail, I'll just give you a quick inference. In Europe, the highest incidence of CJD is in the Netherlands with 1.04 cases per million persons. This compares to the United Kingdom with an incidence of .93 per million cases where you have the presence of the epidemic in cattle. And this is what makes the issue so complex, Mr. Chairman. This is why it becomes even an emotional issue among scientists that discuss the broad implications.

In summary, Mr. Chairman, BSE is complex. It's characterized by a long incubation period and a causative agent that has never been positively identified. The same can be said for CJD. Those who advocate a ruminant-to-ruminant feed ban are reacting to BSE

based on a hypothesis that the disease resulted from the consumption by cattle of meat and bone meal contained in a scrapie like infectious agent. This is not conclusive. It is suppositional.

Since time immemorial, Mr. Chairman, we have been feeding meat and bone meal in the United States, which begs the obvious question. Why have we not had a case of BSE in the United States?

Mr. Chairman, my recommendations to the committee on a base of priorities would be this. We would like to see, working together with the industry and the Government, that we come up as an industry—and I will advocate for my industry—instituting a hazard analysis critical control points that we could assist the cattle in American agriculture for the continued safety of the food supply.

Mr. Chairman, I thank you for the opportunity for being here today.

[The prepared statement of Dr. Franco follows:]

Background

My name is Don Franco, Director of Scientific Services of the National Renderers Association. I also serve as an Adjunct Assistant Professor of Medicine at the George Washington University School of Medicine and Health Science in Washington, D.C. My professional career has been devoted to diseases transmissible from animals to man (zoonoses) and food-borne diseases of bacterial origin. My current responsibilities are to direct the scientific activities of the rendering industry and to develop control and preventative measures based on risk analyses that assure the production of safe rendered animal by-products. The assessment of hazards and the identification of controls based on the Hazard Analysis and Critical Control Points (HACCP) principles is an integral part of my professional role.

The National Renderers Association

The National Renderers Association (NRA) was founded in 1933 so renderers could address problems of the industry collectively and to work with government agencies and allied agricultural groups towards the resolution of issues that impact the industry and agriculture. It is from this perspective that I will profile some of the challenges facing the industry as we examine options and policy considerations pertinent to the bovine spongiform encephalopathy (BSE) complex. Although I highlight the immediate relevance to BSE, it is most opportune to heighten the broad and overlapping influence the rendering industry has on agriculture in general -- the substantial nutritional value the finished products such as meat and bone meal and tallow provide to keep animals healthy, as well as the environmentally friendly role the industry plays in safely and efficiently recycling over 100 million pounds of raw material originating daily from

slaughter/processing of livestock and poultry and other diverse supply sources. On an annual basis this amounts to over forty billion pounds, or enough material to fill a truck convoy using all four lanes of a super highway bumper to bumper from New York to Los Angeles. Thus, although the immediacy of potential regulatory policies tend to predominate, be advised that implications for the industry and allied segments of agriculture are broad.

Transmissible Spongiform Encephalopathies (TSEs)

Without a doubt the transmissible spongiform Encephalopathies (TSEs) are complex. Within the past eight years, some of the nation's most renowned research neuropathologists have described scrapie, the prototype of the TSEs, as viruses. Today, we are aware that current knowledge does not support that causative theory. More is unknown than known, however. As a result, our industry advocates extreme caution before any modification of existing policy, and strongly recommends that the evaluation of regulatory options by the Food and Drug Administration (FDA) be based totally on science, and not on public perception or political expediency. If FDA deviates from risk-based science, a precedent could be established that we may all ultimately regret. One only needs to review the aftermath of the recent disastrous BSE panic in the UK to get a graphic example of this point in its extreme. It is widely recognized that TSEs will continue to challenge the medical and research ingenuity of the most advanced industrialized societies. A hurried effort to policy changes and proposed new regulations will not alter the existing complexities associated with this group of diseases. Now is the time to be rational and objectify priorities to establish reasonable prevention and control

strategies that have worked so well for our country in the last decade to prevent an outbreak of BSE in the United States.

The cause of the bovine spongiform encephalopathy (BSE) remains unknown. All of the current inferences are hypotheses. There have been broad differences of opinions within the scientific community. There is absolutely nothing that approaches consensus. Debate and dissent remains constant. Research findings tend to contradict and cloud any potential resolution of the issue in the immediate future. There is also absolutely no proven evidence aside from epidemiological analogies to associate scrapie to BSE or BSE to Creutzfeldt-Jakob Disease (CJD). Thus, a pressing need for continued research is absolute.

The causative TSE agent for BSE in the United Kingdom is suspected to be from either scrapie infected sheep or cattle with a previously unidentified TSE. Scientists in Europe believe that changes in rendering practices in the UK allowed the TSE agent's survival in meat and bone meal. However, again I must stress that no scientific evidence has been developed to date that proves either of these theories conclusively.

After the initial outbreak of BSE in the UK, the U.S. rendering industry, working in cooperation with the U.S. government and related industries, committed itself to a voluntary ban of specified offal from sheep because of early indications that sheep could possibly be an associative link. The logic was simple, that is, a possible link should be eliminated if at all possible. Since scrapie is present in the United States, albeit at low levels, the industry thought it was both prudent and reasonable to develop an industry policy to ban the rendering of specified offal from sheep. However, a voluntary ban has limits and the industry has no way of guaranteeing compliance. A mandatory ban would

make this a matter of U.S. law, which we believe would increase compliance. In addition, the rendering industry is prepared to develop an internal certification program that can be approved and audited by the FDA.

We believe a ruminant to ruminant feed ban makes sense and is warranted for countries with BSE because the infective TSE agent is present in the cattle population and could lead to further transmission. Such a policy for BSE countries is both prudent and responsible. The USDA's surveillance program tells us that there is no BSE in the United States (almost 2,800 brains from suspect cattle in 43 states have been examined). Without the infective agent present the risk of BSE is lower. Countries without any evidence of BSE are therefore in a different risk category and should be treated differently. Requiring a ruminant to ruminant feeding ban for lower risk countries, like the United States, is not based on current scientific evidence and is premature in our judgment. We believe the focus should be on eliminating the possible infective TSE agent that is present today in our country (i.e. scrapie). This is why we support a mandatory specified sheep offal ban and a mandatory scrapie eradication program with producer indemnification.

BSE: Ruminant-Derived Protein of Scrapie Origin - A Possible Epidemiological Link

A UK rendering practice consistent with the onset of BSE was the widespread discontinued use of the organic solvent extraction procedure in the rendering. This secondary process was sometimes applied to recover tallow which remains in the "greaves" (cracklings) after cooking and removal of free-run tallow. This process provided for an additional yield of tallow by recovering much of the residual fat.

In 1975, approximately 65 percent of the meat and bone meal produced in the United Kingdom was manufactured by solvent extraction methods; by 1982 this proportion had decreased to about 10 percent. This modification, over the period described, is the most convincing linkage to the emergence of BSE. Together with the significant shift from batch to continuous rendering to achieve savings in energy costs, and the use of lower processing temperatures, clearly established this logical associative theory for the initial outbreak of BSE. It is uniquely British, and provides strong circumstantial evidence of the association between BSE and the consumption of meat and bone meal manufactured by procedures which did not include solvent extraction; no other plausible hypothesis/theory has been proposed.

A further relevant factor in the genesis of BSE in the UK was an increase in the sheep population in Britain during the late 1970s and early 1980s, accompanied by an increase in the number of scrapie cases. Both of these significant correlates do not exist in the United States. Also, the UK has never formally instituted scrapie control measures, unlike the U.S. which has had traditional control programs for over 30 years.

The Prion Concept

The transmissible spongiform Encephalopathies in animals and humans are associated with unconventional infectious agents with unusual properties. They are filterable and replicate like viruses, but they differ markedly from viruses in their resistance to physical and chemical treatments that will normally inactivate conventional viruses. The infectious agents are also characterized by their failure to elicit and immune or inflammatory response that are typical of viruses. A distinct structure first observed by Merz and coworkers and associated with the replication of unconventional agents in

the brains of scrapie-infected mice was designated scrapie-associated fibril (SAF), an amyloid protein. SAFs are traditionally found in diseases associated with unconventional agents and have become a significant distinguishing factor in the diagnosis of these complex diseases. Prusiner and coworkers of the University of California, San Francisco, isolated the major protein of SAFs in 1982. He demonstrated in research findings that the scrapie associated protein (SAP), later abbreviated PrP (Prion protein), is the molecule that transmits infection of the transmissible spongiform Encephalopathies.

The Public Health Pertinence of TSEs

The global epidemiology of CJD is that of a randomly disperse disease with an annual overall incidence of about one case per two million people, usually higher in urban than rural areas. It is a presenile dementia found throughout the world, except in rare instances in which the infectious agent was inadvertently transmitted, like in a contaminated corneal implant. The mode of transmission of the disease is unknown. CJD belongs to the broad group of TSEs seen in animals and humans, and is the most significant human prototype of the prion diseases. The disease occurs more or less in a very uniform manner throughout the world, regardless of the occurrence of BSE or scrapie. In Europe, the highest incidence of CJD is in the Netherlands at 1.04 cases per million person-years and no incidence of BSE. This compares to the UK with an incidence of 0.93 cases per million and the presence of BSE as an epidemic in cattle.

The Chairman and Vice-Chairman of SEAC in an open letter of December 13, 1995 stated "that if there ever were any risk to human health from BSE, and there may be none, it was very much less in December 1995 than it had ever been."

On March 20, 1996, SEAC announced their concern of a new clinical course of disease observed in ten patients that was distinct from those usually seen in sporadic or classical CJD. The cases, later designated, Variant-Creutzfeldt-Jakob Disease (V-CJD) were characterized by having remarkably low ages at onset (median 27.1 years) and other atypical features, including a generally protracted and unusual clinical course.

The occurrence of this newly recognized clinic-pathological variant in the UK suggests a new risk factor and prompts discussion as to whether these cases of human prion disease were triggered by exposure to bovine prions, although there is no direct evidence for this so far. A prevailing assumption is that these new cases (a total of 10) may relate to exposure in the mid to late 1980s, before the specified offal ban went into effect.

Discussion/Summary

BSE is a complex disease, characterized by a long incubation period and a causative agent that has never been identified. The same can be said for CJD. Those advocating a ruminant to ruminant feeding ban are reacting to BSE based on the hypothesis that the disease resulted from the consumption by cattle of meat and bone meal containing a scrapie-like infectious agent. This is not conclusive. It is suppositional. There have been reports of animals that have died of BSE in the UK that were never fed meat and bone meal. Since "time immemorial" we have been feeding meat and bone meal in the United States, which begs the obvious question, why have we not had a case of BSE in the United States? The prevailing opinion of epidemiologists is that the risk factors for BSE in the United States are much lower. This theory is based on

an extensive risk analysis published by the Animal and Plant Health Inspection Service's Centers for Epidemiology and Animal Health (CEAH) in Fort Collins, Colorado.

No scientifically validated evidence exists indicating BSE can be transmitted from animals to humans.

In the past, research initiatives in industrialized nations have provided answers to difficult questions challenging the veterinary and medical professions. This lesson should not be forgotten. BSE and CJD provide ample opportunities for both groups to work collaboratively to find answers to these complex diseases. BSE has presented us with a novel neurodegenerative disease related to a poorly understood type of transmissible infectious agent. CJD, in contrast, has been well defined and epidemiologically described in the medical literature for years, but like BSE, the causative agent remains unknown, and, therein, lies the challenge and the problem.

Our priorities must include continued epidemiological studies of the animal and human transmissible encephalopathies, molecular biological studies to develop a test that accurately detects infection in the live animal, and development of improved strain typing methods to assist epidemiological tracing.

Any proposed changes to existing regulations on the feeding of animals should be approached with caution and must be based on science.

Mr. SHAYS. Thank you, Dr. Franco. It's important that you are here, and I appreciate your statement. I think we'll have an interesting dialog. It will be educational to me and Mr. Towns and to the Congress at large. Thank you for coming.

Mr. Hahn.

Mr. HAHN. Good afternoon. I'm Robert Hahn, director of legal affairs and research for Public Voice for Food and Health Policy. Public Voice is a nonprofit consumer organization that seeks to ensure a safe, nutritious, and affordable food supply. I'm testifying today as a consumer advocate concerned about the threat of bovine spongiform encephalopathy.

BSE, as we've heard, is a complex matter. And most Americans are too busy to take the time to educate themselves about it in any depth. They simply assume that the Government will protect them from this apparent danger.

Since learning about the possible connection between BSE and Creutzfelt-Jakob disease, we have been trying to satisfy ourselves that the Government is doing everything it can to make sure that BSE never becomes an American problem. Much of what we've learned has reassured us. However, some important gaps still remain in this country's preventive strategy. And the lack of a ruminant-to-ruminant ban is foremost among them.

As far as we know, BSE does not exist in this country. However, as Britain's recent experience indicates, if BSE ever were to enter the United States, the consequences would be grave. Therefore, we believe that the strongest preventive measures, as part of a comprehensive preventive strategy, are warranted.

Last week, we recommended seven steps that we think should be part of that preventive strategy. Three of our recommendations pertain to FDA. In addition to the ruminant-to-ruminant ban, we recommended that FDA should, one, review rendering practices and mandate those practices that will be most effective for inactivating the scrapie and BSE agents.

And, two, FDA together with USDA should appoint an independent outside panel with a primarily public health orientation to analyze and evaluate all facets of our BSE prevention strategy.

The ruminant-to-ruminant feed ban is critical. The evidence from Britain suggests that feed made from infected ruminants is the primary mode of transmission of BSE. The World Health Organization has called on all countries to enact such a ban and the American Veterinary Medical Association, the National Cattlemen, and several other organizations have called for a voluntary ban until FDA can issue a mandatory one.

Why do we need the ban if BSE does not exist in this country? For one thing, our borders are not hermetically sealed. For example, the United States imports an average of 1 million cattle a year from Mexico, which are slaughtered and rendered here. Even if we succeed in excluding BSE at our borders, USDA has acknowledged that there is a risk, albeit a very small one, of BSE arising in U.S. cattle.

Public Voice believes that time is of the essence in implementing the ruminant-to-ruminant ban. If BSE were to enter the U.S. herd, existing conditions could allow it to spread rapidly. In fact, USDA has stated that the "risk of amplification" would be "much greater"

here than in Britain. That's because meat and bone meal made from cattle make up such a large share of total meat and bone meal produced in the United States

A full FDA rulemaking process would take about a year and a half. We appreciate the need for FDA to act only after due deliberation, but we are concerned about even the perception that FDA has not moved quickly enough. We would prefer an interim or temporary ban pending completion of the rulemaking process. We think that FDA could invoke the good cause exception to dispense with notice and comment procedures under the Administrative Procedure Act.

If this is not possible, we would urge Congress to pass legislation exempting FDA from the notice and comment requirements.

The BSE experience also demonstrates the need for a strong, well funded FDA. In recent years, FDA's resources in most areas have shrunk or remained static as its responsibilities have increased. As the BSE crisis in Europe demonstrates, consumer confidence in the safety of food can evaporate almost overnight if Government is seen as unable to cope with a health hazard. The only way to prevent that here is to ensure that FDA is a strong, well funded and well staffed agency, so that it can fulfill its primary mission: protecting the public health. Thank you.

[The prepared statement of Mr. Hahn follows:]

Good morning. My name is Robert Hahn, Director of Legal Affairs and Research for Public Voice for Food and Health Policy, a national nonprofit consumer research, education and advocacy organization that seeks to ensure a safe, nutritious and affordable food supply for all Americans.

Public Voice has worked for a number of years on meat and poultry safety and has been an active participant during the rulemaking process for the Department of Agriculture's (USDA) much-anticipated Pathogen Reduction/HACCP regulation.

I am testifying today as a consumer advocate concerned about the threat of bovine spongiform encephalopathy (BSE). BSE is a complex matter, and most Americans are too busy to take the time to educate themselves about it in any depth. They simply assume that the government will protect them from this apparent danger.

Since learning about the possible connection between BSE and a new variant of Creutzfeldt-Jakob disease (CJD), we have been trying to satisfy ourselves that the US government is doing everything it can to make sure that BSE never becomes an American problem.

Much of what we've learned about the US response to the threat of BSE has reassured us. However, we believe a few important gaps still remain in this country's preventive strategy, and the lack of a "ruminant-to-ruminant ban" is foremost among them.

THE US NEEDS A COMPREHENSIVE STRATEGY TO PREVENT BSE

Public Voice strongly believes that the government should err on the side of caution in dealing with the threat of BSE. As far as we know, BSE does not exist in this country, and currently there is no cause for alarm. However, as Britain's recent experience indicates, if BSE ever were to enter the United States, the consequences would be grave. Therefore, we think the strongest preventive measures, as part of a comprehensive preventive strategy, are warranted.

Last week, in separate letters to Secretary of Agriculture Dan Glickman and Food and Drug Administration (FDA) Commissioner David Kessler, Public Voice recommended seven steps that we think should be part of that preventive strategy. (A copy of our letter to David Kessler is attached to this testimony.) Three of our recommendations pertain to FDA. In addition to the "ruminant-to-ruminant" ban, we recommended that:

(1) FDA should undertake a review of rendering practices in use in the United States, and should mandate rendering practices-- including procedures to prevent cross-contamination-- that will be most effective for inactivation of the scrapie and BSE agents; and

(2) FDA, together with USDA, should appoint an independent panel with a primarily public health orientation consisting of experts from outside government, and including consumer representation, to conduct an independent analysis of the situation and evaluate all facets of our BSE-prevention strategy.

According to FDA officials, the Center for Veterinary Medicine (CVM) intends to review rendering practices and to determine whether FDA has the legal authority to regulate rendering methods. CVM also intends to issue a "ruminant-to-ruminant" ban but will go through normal notice and comment procedures, possibly starting with an advance notice of proposed rulemaking.

THE "RUMINANT-TO-RUMINANT BAN" IS AN ESSENTIAL ELEMENT OF THAT STRATEGY

The "ruminant-to-ruminant" feed ban is critical, because the evidence from Britain suggests that infected feed is the primary mode of transmission of BSE-- that is, BSE is spread by cattle eating animal protein supplements made from the offal of BSE-infected cows or scrapie-infected sheep.

Recognizing this, the World Health Organization has called on all countries to enact such a ban. Subsequently, the American Veterinary Medical Association, the National Cattlemen's Beef Association and several other producer and veterinary organizations have called for a voluntary "ruminant-to-ruminant" ban until FDA can issue a mandatory one.

In its systems analyses of the BSE hazard, USDA identified "incorporation of infectious material into animal protein products" as one of three critical control points at which the hazard can be controlled; the "ruminant-to-ruminant" ban would be an effective control measure.

Why do we need the ban if BSE does not exist in the United States? For one thing, our borders are not hermetically sealed. For example, the US imports one million cattle a year from Mexico which are slaughtered and rendered here. Even if we succeed in excluding BSE at our borders, there is still a risk, however slight, of BSE or another spongiform encephalopathy arising in US cattle. USDA has acknowledged that there is a risk, albeit a very small one, of scrapie-induced BSE in the US. There is also a theory, not yet ruled out, that BSE occurs naturally in some small percentage of cattle.

If BSE were ever to come here, it would pose an insidious threat because it might not be immediately detected. BSE has a long incubation period, and infected cattle are asymptomatic

until the later stages of the disease. In Britain, it is believed that cattle became infected in 1981-82, but the disease did not appear until 1985-86, a four-year lag. Moreover, if any US cattle were to contract BSE, USDA has stated that the "risk of amplification" would be "much greater" here than in Britain. That is because meat and bone meal made from cattle makes up such a large share (59%) of total meat and bone meal produced in the United States.

THE "RUMINANT-TO-RUMINANT" BAN SHOULD BE IMPLEMENTED AS SOON AS POSSIBLE

Public Voice believes that time is of the essence in implementing the "ruminant-to-ruminant" ban. We feel some sense of urgency, because, in the unlikely event that BSE or some other spongiform encephalopathy were to enter the US cattle herd, existing conditions could make it possible for it to spread rapidly. As previously stated, we believe a comprehensive preventive strategy is called for, and a "ruminant-to-ruminant" ban is perhaps the single most important element of that strategy.

If FDA goes through a full rulemaking process beginning with an ANPR, it would take about a year and a half to issue a final rule. At a minimum, since FDA proposed a rule banning adult sheep tissue in ruminant feed in 1994, and has the benefit of public comments with respect to that similar proposal, it should at least forego publication of an ANPR in this case. We appreciate the need for FDA to act only after due deliberation, but we are concerned that there should not even be the perception that FDA has not proceeded with appropriate speed.

We would prefer to see FDA issue an interim ban pending completion of the rulemaking process. We think that FDA could make a persuasive case that it has "good cause" to dispense

with notice and comment procedures, under section 553(b)(B) of the Administrative Procedure Act (APA), on the grounds that delaying implementation of the ban would be "contrary to the public interest." If this is not possible, we urge Congress to pass legislation exempting FDA from the requirements of the APA in this case.

BSE SHOWS THE NEED FOR A STRONG FDA

Finally, we think that the BSE experience demonstrates the need for a strong, well-funded FDA. It has been well-documented that, in recent years, FDA's staff and resources in this area have shrunk as its responsibilities have increased.

As the BSE crisis in Europe demonstrates, consumer confidence in the safety of food can evaporate almost overnight where there is a significant health hazard and the government is perceived to be unwilling or unable to cope with it. The only way to prevent that from happening here is to ensure that FDA, and especially the centers with responsibilities related to food safety, are strong, well-funded, and well-staffed, so that they can fulfill their primary mission: protecting the public health.

I appreciate the opportunity to testify at this hearing, and I will be happy to answer any questions you may have. Thank you.

PUBLIC VOICE FOR FOOD & HEALTH POLICY
1101 14th Street, N.W.
Suite 710
Washington, D.C. 20005
202 371-1840 FAX 202 371-15
Mark S. Epstein, President

April 30, 1996

The Honorable David A. Kessler
Commissioner
U.S. Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Dear Commissioner Kessler:

Public Voice for Food and Health Policy has been intensively researching bovine spongiform encephalopathy in recent weeks. I am writing to share with you a list of recommendations we feel are in the best interest of the federal government, the domestic food industry, and American consumers. A similar letter is being delivered to Agriculture Secretary Dan Glickman.

Public Voice believes that the federal government should err on the side of caution and take effective preventive measures to make sure that BSE never becomes an American problem.

We know from the steps that FDA has already taken that you also believe that a vigorous preventive effort is called for, and we feel that FDA deserves praise for its efforts to date. As far as we know, BSE does not exist in US cattle. However, the BSE situation is an evolving story, and we think it is necessary to periodically reevaluate our prevention program.

Given the lack of understanding of the disease-causing agent, the difficulties of surveillance and the severity of the disease, we ask USDA and FDA to create several layers of protection for US consumers.

Specifically, we recommend that:

1. FDA should expedite its ban on ruminant protein in ruminant feed. If possible, it should issue an interim ban pending completion of the rulemaking process. If research reveals that BSE is transmissible by oral exposure to swine or poultry, the ban should be extended to ruminant protein in swine and poultry feed.

2. FDA should expeditiously undertake a careful review of rendering processes currently in use in the US. FDA should ensure that the rendering process is changed to incorporate methods that are most effective for inactivation of the scrapie and BSE agents, based on research in the US and Europe. In addition, FDA should mandate procedures in rendering facilities to prevent cross-

contamination. Because of the long incubation periods for scrapie and BSE, asymptomatic but infected animals may be sent to slaughter plants and their offal rendered.

3. USDA and FDA should appoint an independent panel with a primarily public health orientation consisting of experts from outside the government, and including consumer representation, to evaluate all facets of our BSE-prevention strategy, similar to the Spongiform Encephalopathy Advisory Committee in Britain. Currently, USDA's Animal and Plant Health Inspection Service (APHIS) is the lead agency responsible for overseeing our national strategy, because BSE has not yet been proven to be a human health hazard, and APHIS has made a laudable effort to coordinate with its sister agencies. Because of the way food safety responsibility is currently divided, different facets of our national strategy are being handled by different federal agencies. We believe, however, that it would be prudent to have a panel of both human health and animal health experts, independent of both government and the affected industries, charged with the task of conducting an independent analysis of the BSE situation as well as reviewing and assessing the government's entire effort. Such a panel would augment, not replace, APHIS as the lead agency. We think the involvement of human health experts is essential, because, until we know without qualification that there is no relationship between BSE and Creutzfeldt-Jakob disease, we must assume that BSE is a potential human health problem.

4. USDA's Food Safety and Inspection Service (FSIS) should ban specified sheep offal (i.e., brain, spinal cord, thymus, spleen, tonsils, lymph nodes and intestines) from human food. FSIS should also ban cow brain and spinal cord from human food. Current regulations only ban the spinal cord from human food if it has been removed during slaughter. FSIS should require removal of the brain and spinal cord from cattle during slaughter.

5. FSIS and APHIS should expand their surveillance of US cattle with central nervous system disorders as quickly as possible to be sure that BSE does not exist in this country. If and when a diagnostic test is developed that can detect pre-clinical BSE in live cattle, APHIS should test a statistically valid sample of high-risk live animals in a given population or, if feasible, in the entire country. APHIS is now in the process of training FSIS veterinarians, private practice vets, and cattle producers to recognize the symptoms of BSE. APHIS and FSIS are also sampling brain tissue from cattle with central nervous system disorders presented for slaughter at certain plants (selected because of the large number of older cull cows they slaughter); their goal is to gradually expand this so that a sample would be taken from any cattle with a CNS disorder presented for slaughter at any plant in the country.

6. FSIS and APHIS should ensure that countries that export beef and cattle to the US, such as Mexico and Canada, have reliable surveillance programs in place and communicate with these countries to ensure that their domestic herds remain free of BSE. According to the World Health

Organization, "in the absence of surveillance data, the BSE status of a country must be considered as unknown."

7. Congress should appropriate the funds needed for USDA and FDA to take the measures outlined above. Funding for FSIS' BSE-prevention responsibilities must not be taken out of FSIS' budget for postmortem inspection and implementation of the Pathogen Reduction/HACCP regulation.

The above list of recommendations may not be comprehensive; there may be other recommendations we will wish to advance later as we learn more about this issue. We feel confident, however, making these recommendations now.

I welcome your input and hope that we can work together on this issue. I look forward to your response.

Sincerely,

Mark S. Epstein
President

Mr. SHAYS. This is a very interesting panel, because, Dr. Franco, in one sense, you stand on one side of this issue, obviously. So it must be a little frustrating for you because you have four voices that may be going in a different direction. But you're a tough guy.

What I'd like to first get a sense of—and I really wish I had pursued it with our first witness. I'm going to ask you, Dr. Crawford, because you were part of FDA. If there was a very serious public health issue—let me back off and say, basically we have the FDA asking for advance notice of proposed rulemaking. That's a process that tends to take about how long?

Mr. CRAWFORD. Well, in my experience, Mr. Chairman, it has taken from 2 years to 27 years.

Mr. SHAYS. That's fair. That's an honest answer. You have a lot of credibility with me. But if, in fact, it was determined to be a potentially very serious health issue involved—I mean this is—but one in which we couldn't wait even 12 months, what special rulemaking does FDA have that would jump that.

Mr. CRAWFORD. There are several mechanisms they could use. They could require emergency rulemaking and put in a ban immediately. For instance, the way that would work is they would say, perhaps today, May 10, that effective June 1, ruminant-to-ruminant feeding will be banned. And we will take 30 days of comment after that time. But whatever date they stipulated—and they probably wouldn't do it overnight, because existing stores of animal feed would have to be dislodged from the feeding troughs and so forth.

The other thing they could do is they could say this is an emergency rule and we're putting it into effect. I think a limit there is 15 days. It becomes immediately effective. And there is no notion of it being an interim or temporary ban.

Mr. SHAYS. So, fortunately, we do have the capability in instances.

Mr. CRAWFORD. Yes. May I just add one caveat?

Mr. SHAYS. Sure.

Mr. CRAWFORD. I tried to do that in 10 years in my role in the Government, probably seven or eight or nine times, and never was able to do it. And the reason is that the standard of science is so high for those kinds of things, it must be true that there is almost no referent organization or expert who says, this may not be a good idea. You have to fight a couple of battles if you're Dr. Sundlof, which I used to be here. He was on the first panel, the man from Veterinary Medicine.

Mr. SHAYS. Right.

Mr. CRAWFORD. He would have to get through his own leadership. He would have to get through his department. He'd have to get through the OMB, which I've batted about 100 with. Actually, I bat 0 for 0 for this sort of thing.

But I think it would be very hard to do the emergency rules unless there was common agreement.

Mr. SHAYS. That's a very helpful answer. What I would like to ask of each of you is just for you to state where you stand on this. If you were in the position of FDA, would you ask for an immediate ban and go through that process? Dr. Murphy.

Dr. MURPHY. Yes.

Mr. SHAYS. Dr. Crawford.

Mr. CRAWFORD. Yes.
Mr. SHAYS. Dr. Weber.
Mr. WEBER. Yes.
Dr. FRANCO. No.
Mr. SHAYS. Mr. Hahn.
Mr. HAHN. If I could give a slightly longer answer? What we're asking is not that FDA act overnight, not issue a ban overnight; but that they sit down with the affected industries.
Mr. SHAYS. I want to know your answer and then I'll let you qualify it.
Mr. HAHN. Yes.
Mr. SHAYS. In other words, would you like to see an immediate ban in the process?
Mr. HAHN. Yes.
Mr. SHAYS. Now, that's pretty significant, the four of you making that position and, Dr. Franco, I'm going to have you respond in a second. But you may for different reasons or the same reasons explain to me now in a very succinct way why you would have the ban be immediate.
Dr. MURPHY. To err on the side of safety. To not take any further chance.
Mr. CRAWFORD. I would echo that. The situation in England was that they didn't have BSE, either. And it sort of sprung up on them. And you don't really know where it came from. And I think this is an extra measure of safety.
Mr. WEBER. Putting the immediate ban in place does not preclude, and we view would actually accelerate dialog between the industries, the scientists, and the Government, to put in place the type of hazard analysis and critical control point structure that we're moving toward in every other sector of our industry, and that the rendering industry supports that passive approach. The ban would not prohibit—in fact, I think it would accelerate the development and implementation of a passive based system, which is what we need.
Mr. SHAYS. I'll come back to you. Mr. Franco, your answer was no, so let me just come back to you in 1 second. I'm going to give you as much time as you need. Mr. Hahn, you can qualify your answer now.
Mr. HAHN. We feel that there is some sense of urgency because, until disproved, we have to assume that BSE does pass to people. I think the British scientific advisory committee said that that's the most plausible explanation at this time for the 10 case cluster in Britain. It is a fatal disease. And although, hopefully and probably it will never come to this country, I think that we can't make that assumption. We have to adopt measures now.
Mr. SHAYS. Dr. Franco, why don't you respond to what you're hearing?
Dr. FRANCO. Mr. Chairman, first, I don't feel in any way intimidated by being the minority opinion.
Mr. SHAYS. That's good.
Dr. FRANCO. I was very comforted by that. What I would like to share with my colleagues, I heard a comment made erring on the side of safety. I would like my colleagues to say, why don't we err on the side of science. That's what I've been pleading for.

Mr. SHAYS. We're going to pursue that, because I'm going to ask the same question of me in a second. I didn't think you would really feel intimidated, but sometimes I know when I've been outnumbered on a panel, you'd like your story to be heard and not once every shift time. That's what I meant.

BSE, basically you would say it's premature and you would say, let science rule on this issue. And there is an argument for that. There also is the question of, what would you do, would you wait for a BSE outbreak to take place here, a CJD here, in other words, in humans? And is it possible to have scientific consensus ever?

I mean, in other words, I wonder what will it take. I'd love for you to respond to that.

Mr. FRANCO. Mr. Chairman, we still do not know the cause of scrapie. All members on the panel talked about the complexity. Scrapie has been in the literature, I know, in Europe over 150 years. It's been described systematically in the literature. It's so very complex. But, Mr. Chairman, I think more important we need to go back to what we call relative risk.

The risk factors in the United States were well defined by the Department of Agriculture and in the plant held inspection service. The risk factors do not parallel what we have in the United Kingdom, Mr. Chairman. We've been trying to profile that perspective, probably without success.

Mr. SHAYS. I just wonder, though. From my mind, it's kind of probably a classic question of, where does the public health and safety, what trips that in terms of fairness to your industry.

In your business, you don't just supply. The ruminant-to-ruminant feeding is part of your business, correct?

Mr. FRANCO. Sure.

Mr. SHAYS. You take the animal parts and use them in a whole host of whatever.

Mr. FRANCO. Sure.

Mr. SHAYS. Of that, how much is used for feed?

Mr. FRANCO. The ruminants, Mr. Chairman?

Mr. SHAYS. Yes, in your business, in your industry.

Mr. FRANCO. Probably about 15 to 16 percent, strictly to ruminants.

Mr. SHAYS. So, basically, in terms of its impact on the industry, this could be significant given its 15 to 16 percent. But there are clearly other uses that would be nonfeed?

Mr. FRANCO. Yes.

Mr. SHAYS. From your standpoint, Mr. Weber, it would strike me that even if there isn't this scientific—clear, scientific consensus, why take the chance in an industry that's $165 billion when I would gather—and I'd like you to tell me—I would gather that this kind of feed is a very small part of the total amount of feed that is used.

Mr. WEBER. These proteins, which are very high value in high producing animals, excellent sources of amino acids, are used in some cattle diets for those animals with a very high demand for protein. But we do have alternative proteins which can meet those needs. And we will, as producers, pay for this decision. It will cost us money. And we've analyzed that. It ranges between $6 a head

and $30 a head, depending on the scope of this and how all of the adjustments are made.

It will cost producers money. We are well aware of that.

Mr. SHAYS. You represent the industry. So you're the spokesman for a very large industry.

Mr. WEBER. Yes.

Mr. SHAYS. Is there a consensus? I mean, do you come to this meeting, this hearing today, fully aware that this kind of question would be asked and have the authority to make this on behalf of the industry?

Mr. WEBER. Our leadership met probably about 4 months ago and discussed this. And then a decision was made in early March by the leadership of the organization, the producers that I work for, unanimously that this decision would be made.

Mr. SHAYS. I want you to state exactly what the decision is on the part of your industry.

Mr. WEBER. The decision was made to support a voluntary ban that we would work to implement, and request that FDA move forward with either a ban, or if they feel the science warrants, the development of this type of advance notice of proposed rulemaking. But that's a call that they need to make, but we encourage them to do that.

Mr. SHAYS. But they're very different. What they announced today is a very long process. I mean, that could be 18 months, it could be 2½ years, it could be 3. Between those two choices, what is the preference?

Mr. WEBER. And as I said earlier when you asked that question, yes to a ban today.

Mr. SHAYS. I just want to be very clear.

Mr. WEBER. We think that is appropriate. And we will sit down with industry and the science to work out the details of what type of a system would we need in the United States to provide the level of safety that we feel is warranted to protect the health of our cattle, and, of course, the health of our consumers.

Mr. SHAYS. I'm going to come back to this panel. I would at this time ask my colleague, Mr. Towns, if he has any questions.

Mr. TOWNS. Thank you very much, Mr. Chairman. Also, let me join you. This is very impressive. I'd say this is a very impressive panel in terms of their backgrounds and experiences. And I really agree with the chairman. We thank you for taking the time to come as witnesses before this committee.

Let me begin with you, Dr. Weber. In your testimony, you stated that steps could be taken to eliminate BSE during the processing. Could you sort of briefly describe how that could be done?

Mr. WEBER. There are a number of studies under way or have been completed in Europe, which indicates specific times and temperatures required to inactivate these prions or the disease causing agent. Those need to be replicated, in other words, repeated to find out whether indeed those time and temperature profiles would be effective. And then to try to see whether under commercial conditions, those could be achieved. There is evidence to indicate that they can be inactivated.

Mr. TOWNS. Well, you say they're in the process of doing it; or are you saying it can be done now?

Mr. WEBER. The research has been done. And what some would say, well, before we accept that as fact, let's replicate, let's repeat those studies. But there are very promising studies which indicate that appropriate times and temperatures can inactivate these agents.

Mr. TOWNS. Thank you. I guess to you, well, actually all of you. In your opinion, is the Federal Government exercising sufficient vigilance in monitoring and preventing exposure of U.S. livestock to BSE? Are you satisfied with what's going on? All of you. I'm going to go down the line. Dr. Murphy, we'll start with you first.

Dr. MURPHY. Almost. Having worked at CDC for 25 years, I truly believe in surveillance. The recent announcement from USDA that surveillance would be increased makes me feel good. At this moment, 2,795 cattle have been examined histopathologically, the ultimate test for spongiform encephalopathy. I don't think that's a very big number. There are about 133,000 cattle slaughtered every day in this country.

Mr. TOWNS. How many thousand?

Dr. MURPHY. A hundred thirty-three thousand. I read that in the New York Times last week.

Mr. WEBER. These animals that are being examined are animals that have the symptoms that one might suspect would be spongiform encephalopathy. Our inspection system at plants, Federal and State inspected plants, has a very rigorous inspection program before the animals enter the plant, because we have rabies in this country. And rabies, the behavior, if you've seen any of the videotapes, resembles these types of neurologic problems.

And there's 250 animals a year that the Food Safety Inspection Service will not allow in the plants because of these symptoms. All of those animals are examined. And that's been kind of a beginning of this surveillance program. So they're actually targeting the very animals that you would expect to have this. And over the last 10 years, since 1986, again with the very high risk animals, it has never been identified.

That raises our confidence level significantly, but we still support the additional surveillance that's been proposed by USDA.

Mr. TOWNS. I think Dr. Murphy is saying something else.

Dr. MURPHY. No. I really meant to say the same. In fact, when I was at CDC, all cattle brains coming through as rabies suspects became the first animals that were examined for spongiform encephalopathy. So that's how the surveillance system got started. It got started at CDC and then was adapted by the USDA and its diagnostic labs.

I just think that there is a lot more animals out there that should be examined.

Mr. TOWNS. The sample should be larger you're saying?

Dr. MURPHY. That's what I'm saying. And I think Dr. Weber said the same thing.

Mr. TOWNS. Dr. Crawford.

Mr. CRAWFORD. Yes. I'm like Dr. Murphy. I'm almost pleased. I think that the efforts of the Government when BSE first became fully known to the U.S. Government and also to its stakeholders and livestock industry, the procedures that were put in place ac-

count for the fact that not only do we not have BSE, but we know we don't have it.

So the testing that was done, actually at Dr. Murphy's suggestion, I think gives us the measure of assurance that we need. A little more surveillance and also expediting the FDA process on the ruminant-to-ruminant feeding would make me 100-percent satisfied.

Mr. TOWNS. Dr. Franco.

Dr. FRANCO. I think increased surveillance, we all concur with. That has to be done. And I thought that the animal disease control officials in Agriculture and through APHIS have done a very good job. Even the surveillance program of about close to 3,000 brains, assuming what Dr. Weber said and I know what Gary said is quite right, with a high of 250, is relatively significant. But we could improve on that surveillance program.

Mr. TOWNS. Let me do a followup with you. Do other emerging infectious diseases present these same concerns?

Dr. FRANCO. Congressman, what I alluded to early on is that all of these diseases are so complex that we are all concerned about them. And I don't think—there are many conceptual similarities what we have been seeing here.

My only differences with other members of the panel is whether or not an immediate ruminant-to-ruminant ban is indicated now based on the science. We are equally concerned about the broad serious implications of all of the spongiform encephalopathy. So I do share the panel concerns about the seriousness of the total issue.

Mr. TOWNS. Mr. Hahn.

Mr. HAHN. On the whole, we are satisfied with what the government is doing. But we think there are still some gaps. In particular, the ruminant-to-ruminant ban. There is a need to review the rendering methods in use in this country; and also to expand surveillance.

Mr. TOWNS. I cut you off, Dr. Weber. I cut you off. Did you have anything else you'd like to add? Because I cut you off and went back to the panel.

Mr. WEBER. No.

Mr. TOWNS. Mr. Chairman, I yield back at this time.

Mr. SHAYS. Thank you. I'm just going to ask one or two more questions here. I don't intend to go too much longer.

Dr. Franco, you asked, in essence, as I'm interpreting it, why not err on the side of science. And the answer that I would tend to say is because science finds problems much faster than solutions. I mean, I think we have identified scientifically some very real problems.

So then I'm wondering why we don't work backward, from effect back to cause. The ban preceded a sharp drop in BSE in Great Britain. Is that coincidental? And I would think it is not coincidental.

So my question is, why not do what works until science tells you why it works. In other words, I'm wondering if we have to wait to find out why it works scientifically and if that would be too late.

Dr. FRANCO. But, Mr. Chairman, those are two different environments. It worked in England where you had an incidence of BSE. BSE was active. It was an epidemic form. I think just about 60 per-

cent of the dairies had at least one case of BSE. And I could see that being very applicable for the United Kingdom, because the disease was an active phase within the United Kingdom.

Mr. SHAYS. But there was clearly a connection.

Dr. FRANCO. And the connection was real after the ruminant-to-ruminant ban, Mr. Chairman. You're perfectly correct. The curve, the epidemic curve made a very impressive decline. And I think Dean Murphy alluded to that in his testimony. That indeed the epidemic curve was impressive. I allude to that as being fact and good science.

Mr. SHAYS. Let me ask if any of you would like to make any additional comment. We're not focused on a lot of different issues. And I think your positions are fairly clear and your testimony has been very helpful. Dr. Murphy.

Dr. MURPHY. You asked about consensus, the big umbrella. And, of course, there are never consensus. But I think under the big umbrella, there are several smaller umbrellas. Within the biomedical community, there is almost consensus now on the nature of the prion and what's going on, including lots of very recent research that's really exciting.

It's true that under other umbrellas, there is a lot more caution as you've heard here today.

I think one of the keys is what people think about epidemiologic research. I spent 25 years at CDC, where epidemiology research was always solid but often controversial; if you disagreed with the results, it was seen to be soft. Maybe it's like circumstantial evidence in criminal law.

The epidemiologic evidence does not need to be seen as soft, but it is circumstantial.

Mr. SHAYS. I'm just struck by the sense that, one, the risk could be so gigantic; but risk in terms of, one, public safety. Two, if the industry—I mean, just knowing the fear that some Members of Congress had who are sincerely concerned about this issue not being blown out of proportion. But knowing their concern and knowing if there were any indication, and knowing how sometimes the press works and knowing how a Sunday night magazine featured issue on this could just blow this into an incredible issue for the country, I can understand your concern, Dr. Weber, in terms of what it can lead to.

And I can understand your concern, Dr. Franco, that there may not be a connection that we see. It can be just coincidental. It can be a little more than that. But you want to have it based on real science and you don't want to have your industry harmed based on faulty science. And I can understand that.

I need to ask one other question for the record. And I'm usually reluctant to do this since it introduces a whole new element. I'm not intending to get into great depth on this, but I want to know what is the role in animal genetics in assuring animal health and food safety.

I'd like each of you on the record, if you would. I'm not looking for particularly long answers, but we're going to be pursuing this in future hearings.

Dr. MURPHY. There's a very tight genetic predisposition to scrapie among breeds of sheep. There is no evidence of breed sus-

ceptibility among cattle in Britain. In the human disease, 90 percent of CJD is sporadic, we have no idea what the source is. Ten percent is familial, is genetic.

Mr. SHAYS. Dr. Crawford.

Mr. CRAWFORD. I don't have much to add to that, except there is a variant of Creutzfelt-Jakob disease that is understood to be 100 percent genetic. And that's called Gerstmann-Sträussler-Scheinker syndrome.

Mr. SHAYS. I think I saw that word written down and I decided that's why I wasn't going to ask that question. Dr. Weber.

Mr. WEBER. Relative to genetics, are you referring to animal health in the broadest context?

Mr. SHAYS. Yes.

Mr. WEBER. Certainly, as we learn more about genetics, there are predispositions to a lot of diseases. There is inherent resistance. Recently in the United States we have imported embryos from South America from a breed of cattle that are very resistent to parasites because they have evolved in an environment.

Mr. SHAYS. How about specifically to this issue?

Mr. WEBER. I know of no genetic predisposition at all associated with this.

Mr. SHAYS. With the cattle versus the sheep.

Mr. WEBER. With the sheep one, there is. And with the human variants, there appear to be.

Mr. SHAYS. Dr. Franco.

Dr. FRANCO. Nothing to add to Dr. Murphy's comments.

Mr. SHAYS. But you would agree with them?

Dr. FRANCO. Yes.

Mr. SHAYS. Thank you.

Mr. HAHN. I'm not qualified to speak about genetics.

Mr. SHAYS. That's fair enough. Fair enough. I have no more questions. I don't think Mr. Towns has any more questions. Yes, Dr. Crawford.

Mr. CRAWFORD. This is not completely on the subject, but it's brief. We've taken a poll of this August panel and the vote comes out that the average cow actually—not to disagree with the first panel—but they actually have four stomachs, rather than two.

Mr. SHAYS. You know what? I want to tell you something. I thought it was more than two, but I figured, I've asked such dumb questions, I'm not going to say that.

Mr. CRAWFORD. This is only the average cow.

Mr. SHAYS. Can I say to you that I like having the oversight. I like having the FDA come after we get a broad overview. And I know that probably in your time you preferred to go first when you were with FDA. But it would have been helpful, frankly, to have you all go first and then to have them go second. But it's a courtesy that we extend sometimes very reluctantly. But, thank you. I was going to ask my staff later. I thought you told me they had more than two stomachs.

Mr. TOWNS. I don't know whether you want to pursue it any further, but my staff is saying three stomachs.

Mr. SHAYS. It's more than two. Well, what do we know. Thank you very much.

Our third panel is Dr. Welser; Dr. Sherbyn Ostrich; and Dr. Cindy Wolf. And if all three would come forward? I believe we're going to focus primarily on animal drugs in this last panel.

[Witnesses sworn.]

Mr. SHAYS. For the record, all three witnesses have responded in the affirmative. Dr. Welser, I think we'll go with you first and then we'll go in the order that I called them. So we'll go in this direction. Thank you.

STATEMENTS OF JOHN WELSER, PHARMACIA AND UPJOHN; SHERBYN OSTRICH, AMERICAN VETERINARY MEDICAL ASSOCIATION; AND CINDY WOLF, AMERICAN SHEEP INDUSTRY ASSOCIATION

Dr. WELSER. Thank you, Mr. Chairman. I will summarize my written testimony. Under the guidance of Dr. Sundlof, the Center for Veterinary Medicine has made significant progress in improving its review and approval procedures; thus, making more approved products available, assuring the public that the drugs administered to their animals are safe and effective.

Three areas I will comment on are approval times, manufacturing and surveillance and compliance priorities.

Approval times. I believe that the agency's implementation of the phased review system has significantly improved the approval process. It has provided sponsors with the opportunity to submit data and reach concurrence on sections of a product's application throughout the approval process.

Recently, it resulted in our company receiving an approval in just 2 weeks. They said three. We counted it as two after filing a completed NADA application. This, I'm sure, has set a record within the agency. The total application, though, had been in development for several years.

The point is when more safe FDA approved drugs are available for treating animals, the threat of potential zoonoses is reduced.

The only problem my company has encountered regarding this phased review system has been coordination during the final review process. At this point, some units within the agency second-guess other units or reviewers within the Center and question decisions made earlier in the approval process. This delays approvals. Dr. Sundlof is aware of these problems and is working to correct them.

Currently, we have only one product with which we are experiencing delays. And that is bovine somatotropin for milk production. We initiated research on this product in 1982 and do not expect approval for another few years. Because of the controversy surrounding the use of hormones in milk production, the requirements for approval of this product have become increasingly stringent and subject to a new level of regulatory scrutiny.

It is important that both FDA and the Congress recognize that the decisions about food safety and the approval of veterinary products should be made solely on the basis of science, not media hype or hypothetical fears.

Manufacturing issues. By statute, the Center for Veterinary Medicine has authority over the manufacturing section of the animal drug approval process. However, the FDA district offices have

oversight over the manufacturing facilities. As a result, there are often mixed signals from the Center as opposed to the district offices regarding the manufacturing process. This results in delays, miscommunication and duplication of efforts. It would facilitate the approval process if one group was given the authority over the whole chemistry and manufacturing section.

Surveillance and compliance. It is my belief that the intent of the American Medicinal Drug Use Clarification Act, or AMDUCA, passed by Congress in 1995 was to decriminalize the utilization of drugs in an extra label fashion for those conditions which there were either an inadequate number of approved drugs or no approved drugs available. It was not to encourage the profession to replace approved drugs with unapproved products based on cost or personal perception.

The current emphasis of the surveillance and compliance unit of FDA's Center for Veterinary Medicine is to monitor the activities of companies who market drugs approved for use in animals. A quick review of CVM's proposed strategic plan shows that only 7 of the 79 agenda items listed deal with the surveillance of the marketing and distribution of drugs that are not approved for use in animals.

There needs to be a significant shift in CVM's emphasis to include greater monitoring of the use of drugs that have not been approved for use in animals. An example of this is a human-approved cephalosporin which is being promoted by telemarketing and other means for use in animals. Drugs like this lack data for target animal safety, human food safety, withdrawal periods and drug residue detection. This is why the use of human labeled products in animals, especially when there may be an approved animal drug available to treat the condition, should be troubling both to the FDA and the Congress. I suggest that CVM's surveillance and compliance unit dedicate its resources to monitoring and controlling the level of extra label unapproved drug use.

Everyone agrees that the best solution to extra label drug use in veterinary medicine is to encourage and ensure that a greater number of products are approved and labeled for use in animals. There is currently legislation before the Commerce Committee designed to increase the availability of safe and effective health products. This legislation has received wide bipartisan support in both the House and Senate. And I'm pleased that both of you have supported this act. And it's supported, also by veterinarians, animal drug manufacturers, livestock and poultry groups and the feed industry.

In my written testimony, there are four suggestions to assist the agency in helping to assure proper drug usage. And I will not cover them here.

We believe it was not the intent of the extra label drug law to allow the promotion of human approved drugs for animal uses, except in those conditions where there are no other products available. And we believe it's FDA's responsibility to survey and

monitor conditions, whether you're talking about zoonoses and/or extra label drug use in other conditions, rather than looking at those things that are routine.

Thank you. And I'll answer questions.

[The prepared statement of Dr. Welser follows:]

TESTIMONY
Committee on Government Reform and Oversight
Subcommittee on Human Resources and Intergovernmental Relations
May 10, 1996

John R. Welser, DVM
Pharmacia & Upjohn, Inc.

I appreciate the opportunity to provide testimony regarding FDA's Center for Veterinary Medicine. My name is John Welser, and I am vice president of animal health research and biologics for Pharmacia & Upjohn. My company is based in Kalamazoo, Michigan and our animal health interests include vaccines, pharmaceuticals, and feed additives for both large and small animals. I am a veterinarian and am a former dean of the College of Veterinary Medicine at Michigan State University.

Under the guidance of Dr. Steve Sundlof as director of the Center for Veterinary Medicine, FDA has made significant progress in improving its review and approval procedures for new animal drugs, thus making more products available to practitioners of veterinary medicine, and ultimately assuring the public that the drugs administered to their animals are safe and effective.

In addition, the animal health products industry, in collaboration with veterinary groups, livestock groups and the commercial feed industry, have been working with Dr. Sundlof on creative, responsible solutions to help address inefficiencies in the product approval process.

The three areas I would like to comment on today are approval times, manufacturing issues, and surveillance and compliance priorities.

I believe that the agency's implementation of a phased review system has significantly improved the approval process. It has provided sponsors with the opportunity to submit data and reach concurrence on sections of a product application throughout the approval process. Recently, it resulted in our company receiving an approval just two weeks after filing a completed New Animal Drug Application. This, I am sure, has set a record within the agency. The total application, incidentally, had been in development for several years.

The point here is that when more safe and effective drugs are available for treating animals, the threat of potential zoonoses is reduced.

The only problem my company has encountered regarding this phased review system has been coordination of the review as it enters the final approval phase. At this point, some units within the agency seem to second-guess other reviewers at the Center and question the decisions made earlier in the approval process. This serves to delay approvals and can foster an environment of keeping products off the market, rather than approving new ones. For some companies in the animal health industry, this is a very significant problem. Dr. Sundlof is aware of this and has indicated that he is working to correct these problems.

Currently, the only product with which Pharmacia & Upjohn is experiencing delays is bovine somatotropin for milk production. We initiated research on this particular product in

1982 and still do not expect to see approval for a few years. Because of the controversy surrounding the use of hormones in milk production, it seems that the requirements for approval of this product have become increasingly stringent and subject to a new level of regulatory scrutiny. It is important that both FDA and the U.S. Congress recognize that decisions about food safety and the approval of veterinary products should be made solely on the basis of science, not media hype or hypothetical fears. Using science as the respected criterion for making food safety decisions has kept the United States the recognized leader in food regulation.

The second issue I would like to discuss relates to manufacturing issues. By statute, the Center for Veterinary Medicine has authority over the manufacturing section of the animal drug approval process. Nevertheless, the FDA district offices, which are not administratively responsible to the Centers, have oversight of the actual manufacturing facilities. As a result, there are often mixed signals received from the Center for Veterinary Medicine as opposed to the district offices regarding manufacturing issues. This results in delays, miscommunication and duplication of efforts. It would very much facilitate the development and approval process if one group would be given the authority over the whole chemistry and manufacturing development and approval process. This area has become a major hurdle for animal drugs because standards developed for the manufacturing of human drugs are being readily applied to the manufacture of animal drugs resulting in unnecessary delays.

The final issue I'd like to discuss involves surveillance and compliance priorities. It is my belief that the intent of the Animal Medicinal Drug Use Clarification Act passed by Congress in 1995, was to decriminalize the utilization of drugs in an extra-label fashion, similar to the case

for human drugs, for those conditions for which there were either an inadequate number of approved animal drugs or no approved drugs available. It was not to encourage practitioners to replace approved drugs with unapproved products based solely on costs.

The current emphasis of the surveillance and compliance unit of FDA's Center for Veterinary Medicine is to monitor the activities of drug companies who market drugs approved for use in animals. A quick review of CVM's proposed strategic plan shows that only 7 of 79 agenda items listed deal with surveillance of marketing and distribution of drugs that are not approved for use in animals. There needs to be a significant shift in CVM's emphasis to include greater monitoring of the use of drugs that have not been approved for animal use. An example of this is a human approved cephalosporin which is being promoted by telemarketing and a wide variety of other means. Drugs like this one lack data for target animal safety, human food safety, establishment of withdrawal periods, and drug residue detection analyses. That is why the use of human-labeled products in animals – especially when there may be an approved animal drug available to treat the given condition – should be troubling to FDA and Congress. I suggest CVM's surveillance and compliance unit dedicate further resources to monitoring and controlling the level of extra-label and unapproved drug use, especially in cases when there are approved drugs available.

Everyone agrees that the best solution to extra-label drug use in veterinary medicine is to ensure that a greater number of products are approved and labeled for use in animals. There is currently legislation before the Commerce Committee designed to increase the availability of safe, effective animal health products in this country. This legislation has received wide

bipartisan support in the House and Senate and is supported by veterinarians, animal drug manufacturers, livestock and poultry groups and the feed industry.

In addition to implementing this legislation when it is passed, there are several things FDA can do to address the problem of human-labeled products being used in veterinary medicine.

First, FDA should produce a list of conditions for which there are none or an inadequate number of drugs available to treat the condition where extra-label drugs would be completely appropriate, such as companion animal diabetes.

Second, FDA should produce a list of conditions for which there are an adequate number of approved animal drugs available and extra-label drug use would not be appropriate, such as bovine respiratory disease.

Third, FDA should improve its surveillance of the promotional practices of manufacturers and distributors of drugs that are not approved for animals, but are being used in veterinary medicine. FDA should require distributors to ensure that differentiation is made between approved animal drugs and non-approved animal drugs in their literature and telemarketing efforts.

Fourth, FDA should ensure that the manufacturing processes, inventories, and flow of products is to areas where it is appropriate and use would seem to be warranted.

We believe that it is not the intent of the extra-label law to allow the promotion of human-approved drugs for animal uses, except in those conditions for where there are no other products available. It is FDA's responsibility to ensure that this law is enacted as intended.

In conclusion, I would like to commend Dr. Sundlof for the efforts he is making at the Center for Veterinary Medicine and to stress the importance of enacting animal drug availability legislation to ensure that the products needed to keep animals healthy are available in the marketplace in a reasonable timeframe and at a reasonable cost. Thank you.

Pharmacia&Upjohn

26 June 1996

Animal Health

John R. Weiser, DVM, Ph.D.
Vice President
Research & Biologics

Ms. Anne-Marie Finley
Subcommittee on Human Resources
and Intergovernmental Relations
B372 Rayburn House Office Building
Washington, D.C. 20515

Dear Ms. Finley:

I appreciate the opportunity to testify at the recent hearing to present the Animal Health Institution's point of view on drug residues and food safety. There are two items , however, that were raised during the hearing about which I would like to comment further:

Drug Availability: As you know, we support the Animal Drug Availability Legislation (HR 2508) which will improve procedures in CVM for approving drugs. As a result of this legislation an increasing number of approved drugs will insure that target animal and human food safety issues are satisfied while improving overall Animal Health. As I indicated in my testimony before the Subcommittee, the AMDUCA Law, which permits the veterinarian to utilize drugs off label for the treatment of animal diseases, does not insure human food or target animal safety through clinical study. It simply permits the veterinarian to treat animals with drugs he believes are appropriate when there are not approved drug therapies available to treat the disorder. This provision is being misused by some individuals within the veterinarian profession to reduce costs by utilizing non-approved drugs or human approved drugs based on their own clinical impressions. This undermines the intent of the law and, more importantly, puts in jeopardy the human food supply and target animal safety.

Harmonization: During the hearing the issue of harmonization was raised. This is an extremely important issue since the lack of harmonization of drug approval requirements and processes is often used as a non-tariff trade barrier. An appropriate action may be for the Congress to hold a hearing dealing with this subject and how harmonization might better be facilitated.

9600-190-46
Pharmacia & Upjohn
7000 Portage Rd.
Kalamazoo, MI 49001-0199

Telephone (616) 833-3323
Facsimile (616) 833-2707
Internet ID john.r.weiser@am.pnu.com

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Thank you again for the opportunity to testify before the Subcommittee. I look forward to our continued interaction.

Sincerely,

J.R. Welser

JRW:aw

Finley.Ltr

Mr. SHAYS. Thank you, Dr. Welser. Yes, sir.

Dr. OSTRICH. Mr. Chairman, thank you for this opportunity to speak to this subcommittee regarding the crucial role of the Food and Drug Administration's arm, Center for Veterinary Medicine, to the veterinary profession.

I am Dr. Sherbyn Ostrich. I am president of the American Veterinary Medical Association, which represents 58,000 veterinarians across this country, which is about 85 percent of all of the veterinarians in the United States. The mission of the AVMA is to advance the science and art of veterinary medicine through its involvement in public health, biological science, and agriculture. Members of the AVMA participate in every aspect of veterinary medicine, including companion animals, exotic animals, and food-producing animals.

I am here to speak to you today basically as a companion animal practitioner from Wernersville, PA, although I have been a food-animal practitioner for my first 10 years in practice. The practice I am in now serves 13,000 clients, with the practice limited to companion animals and a few exotic species.

I received my veterinarian medical degree from the University of Pennsylvania in 1963. Since then, I have been active in many facets of organized veterinary medicine, including being elected president of the Pennsylvania Veterinary Medical Association, nationally serving as the AVMA executive board chairman and currently as its president.

I am also a commissioner on the Pennsylvania Health and Diagnostic Commission. The Center for Veterinary Medicine is essential in providing the practicing veterinarian with pharmaceutical tools to maintain and restore animal health. A veterinary skill in diagnosing and treating the family pet also directly, believe it or not, affects the health of the humans owning that pet.

Through monitoring the health of companion animals and educating pet owners in disease communicable between animals and people, veterinarians fulfill one of the many contributions to human health. However, recent reductions in personnel and other resources combined with sometimes duplicative and unnecessary testing and efficacy requirements have resulted in very few new animal drugs being approved.

The significant cost and time required to secure approvals for every use, for every species discourages pharmaceutical companies from undertaking this effort. Let me give you an example. Recently, Merck put on the market a drug called Enacard for use in heart disease in dogs. It costs Merck an extra $25 million to bring that drug to market, although this drug has been on the human market in the generic name of Enalapril, and brand name of Vasotec—the Merck name for it—for many, many years.

And the problem here, basically, is that when it was brought forth for human use, all of the testing and toxicity studies were done in dogs, they had to do it all over again to get it put on the market for veterinary medicine. Now, that should be an addendum to the book that's out now, "The Death of Common Sense."

Mr. SHAYS. Doctor, what we need to do is to test humans so we know it's safe for dogs.

Dr. OSTRICH. I don't think we want to do that. Well, that's what we did in this particular case maybe. The significant cost and time is ludicrous.

The CVM is aware of these problems and has responded recently to this serious shortage of approved drugs for the treatment of animal conditions and has recently taken steps to better ensure the timely review and approval of new animal drugs. In doing so, the CVM must be allowed to ensure that decisions with respect to animal drugs certainly are based on science.

In recognition of the fact that approved animal drugs are not available to many veterinary requirements, the 103d Congress passed the Animal Medicinal Drug Use Clarification Act, which is commonly known as the extra label drug bill. And I differ from my colleague, Dr. Wexler, in that they should do more regulations on that end than on the other.

We strongly feel from the AVMA standpoint that veterinarians are trained professionals and they should be able to use their professional judgment on which drug is best for that patient and follow through with whatever responsibilities they have in the after effects of that drug.

This act will permit veterinarians to use FDA approved drugs for various conditions and in dosages, other than what is specifically indicated on the label; subject, of course, to FDA regulations which are due to be promulgated by October of this year, thus, when a veterinarian administers insulin to an insulin-dependent diabetic dog or cat, or administers a cancer fighting drug to a family's companion animal, that veterinarians will no longer be breaking the law as he or she had been without this legislation. Similarly, this law assists veterinarians in that he or she may now again, under FDA regulations, prescribe or administer medication to minor species, such as sheep, goats, aquatic and exotic animals, even though no approved drug for that specific species or condition presently exists.

While this extra label legislation will be essential to the practicing veterinarian, the overall problem of drug availability still remains. The Animal Drug Availability Act in 1995, as it was mentioned here, has been introduced, and we are in complete support of this legislation.

Mr. SHAYS. Doctor, let me just interrupt you for a second. How much longer is your testimony?

Dr. OSTRICH. Very short.

Mr. SHAYS. Very short in this place can mean anything.

Dr. OSTRICH. I think I can read it out in less than 3 minutes.

Mr. SHAYS. I guess what we'll do is we'll finish with your testimony and then we'll vote. So why don't you finish with your testimony.

Dr. OSTRICH. Another important issue to practicing veterinarians and animal lovers and owners is one of how best to disseminate drug information. Because there is no FDA approval for every drug needed to treat every species for every condition, veterinarians are constantly searching for effective therapeutics to treat the presently untreatable.

Extra label drugs are necessary in those cases where disease conditions are not responding to an FDA approved treatment or those

in cases in which there is still no drug available. Cancer chemotherapeutic agents approved for use in humans are effective in many cancer afflicted companion animals and information on dosing regimens for dogs and cats is often not readily available, even though, again, they had been tested in dogs and cats before they went into humans.

To better treat our patients, it is critical that veterinarians have access to updated information on the use of new products. Oftentimes, the best place to go for this information is to the drug sponsor or veterinary experts. Currently, FDA prohibits the free exchange of information, for example, between veterinarians at sponsored seminars and also between veterinarians and drug sponsors at medical conferences.

Veterinarians with expertise who mention extra label drug uses in the course of a scientific lecture should be allowed to do so as long as any corporate sponsorship toward this lecture is not extravagant and the sponsor does not control the scientific material presented. To me, that is a violation of first amendment rights. I really don't understand that part of the regulations.

Likewise, industry should be able to distribute information to veterinarians, provided the accompanying studies are consistent with a drug being safe and effective. We should encourage FDA and CVM to come forward with much needed guidelines to allow the dissemination of this information.

Ladies and gentlemen, the ultimate raison d'etre of veterinary medicine is the enhancement of human health, as well as animal health. In the interest of time, I'll end here.

[The prepared statement of Dr. Ostrich follows:]

Mr. Chairman, thank you for the opportunity to speak to this subcommittee regarding the crucial role of the Food and Drug Administration, Center for Veterinary Medicine (FDA/CVM) to the veterinary profession. I am Dr. Sherbyn W. Ostrich, President of the American Veterinary Medical Association (AVMA), which represents over 58,000 veterinarians. The mission of the AVMA is to advance the science and art of veterinary medicine through its involvement in public health, biological science, and agriculture. The members of the AVMA participate in every aspect of veterinary medicine including companion animals, exotic animals and food-producing animals.

I am here to speak to you today as a companion animal practitioner from Wernersville, PA. I am a member of a four veterinarian practice. The practice serves 13,000 clients, with practice limited to companion animals and a few exotic species. I received my veterinary medical degree from the University of Pennsylvania in 1963. Since then, I have been active in many facets of organized veterinary medicine, including being elected President of the Pennsylvania Veterinary Medical Association, and nationally, serving as the AVMA Executive Board Chairman and currently as its President.

The Center for Veterinary Medicine (CVM) is essential in providing the practicing veterinarian with the pharmaceutical tools to maintain and restore animal health. A veterinarian's skill in diagnosing and treating a family pet may directly affect the health of humans. Through monitoring the health of companion animals and educating pet owners on zoonoses (diseases communicable between animals and people) prevention, veterinarians fulfill one of their many

contributions to human health. However, recent reductions in personnel and other resources, combined with (sometimes) duplicative and unnecessary testing and efficacy requirements, have resulted in very few new animal drugs being approved. The significant cost and time required to secure approvals for every use for every species discourages pharmaceutical companies from undertaking this effort. The CVM is aware of these problems and has responded to this serious shortage of approved drugs for the treatment of animal conditions and has recently taken steps to better ensure the timely review and approval of new animal drugs. Indoing so, the CVM must be allowed to ensure that decisions with respect to animal drugs are based on science.

I would like to provide this Committee with a brief background surrounding the issue of pharmaceutical use by veterinarians. As a companion animal veterinarian, many of my patients are fighting diseases for which an effective drug may exist, however, if the drug is *not* specifically labeled to treat each condition or aliment, or if the label does *not* list the species in question, then I cannot use that medication to treat my patients. In 1968, the Food, Drug and Cosmetic Act (FD&C Act) was amended to regulate animal drugs. The amendment created a program for approving new animal drugs and incorporated language into section 512 (a) (21 U.S.C. 360b (a)) that limited the use of animal drugs to the specific species and usage directed by the label. Species, uses and dosages not identified -- no matter how safe and beneficial -- were illegal. However, the standard practice of veterinary medicine and the recognized treatment regimens for many diseases have moved ahead faster than the introduction of approved new animal drug products. For example, between 1987 and 1994, only ten novel pharmaceuticals (containing active ingredients which had not been previously approved) were approved by the

FDA for food-producing animals. None were approved for companion animals. The annual research and development costs total nearly $400 million which is almost 18 percent of the $2.4 billion animal health products industry. The average cost of developing just one animal health product, which takes on the average 11 years to bring the product from point of discovery to market, is more than $22 million. Coupled with the fact that nearly 90 percent of all animal health products have annual revenues of $1 million or less, it becomes clear that the significant cost and time required to secure approvals for every species discourages pharmaceutical companies from undertaking this effort for every conceivable scenario in animal medicine. As a result, necessary and efficacious new drug therapies are being kept from the marketplace which, in turn means that the health and well being of both companion and food animals is being placed at risk because there are fewer safe and effective drugs available to treat disease conditions.

Moreover, the animal health products industry is very small when compared to the human prescription pharmaceutical sales -- $2.3 billion for animal health products compared to $51.3 billion for human prescription drugs-- but from a veterinarian's point of view this industry is vitally important if he or she is going to be able to provide complete medical care for their patients. An anesthetic which is labeled for uses in cattle and horses, may be equally safe and effective for sheep, dogs and cats, but currently cannot be used in these additional species legally by a licensed veterinarian because they are not listed on the label. Accordingly, the strict enforcement of the FD&C Act would have made it impossible for veterinarians to practice medicine in a modern and scientific manner when they are forced to rely on a limited field of approved medications to treat their patients.

In recognition of the fact that approved animal drugs are not available for many veterinary requirements, the 103rd Congress passed, and the President signed on October 7, 1995, the Animal Medicinal Drug Use Clarification Act of 1994 (P.L. 103-396). This act will permit the veterinarian to use FDA approved drugs for conditions and in dosages other than what is specifically indicated on the label (extra-label), subject to FDA regulations which are due to be promulgated by October of this year. I might add that the passage of the extra-label drug bill evolved over a protracted political process that began in the mid-1980s and which involved the active participation of the AVMA, individual veterinarians, humane organizations, livestock producers, pet owners and others.

Some of the key provisions of Animal Medicinal Drug Clarification Act of 1994 regarding the use of animal drugs are:

- Extra-label use of FDA-approved animal drugs will be permitted under the following conditions: (i) by or on the lawful written or oral order of the licensed veterinarian; (ii) within the context of a veterinarian/client/patient relationship*; (iii) in compliance with regulations promulgated by the Secretary of Health and Human Services.
- Extra-label use of animal drugs in or on animal feed is not permitted.
- The Secretary may prohibit particular uses of an animal drug.
- Extra-label use of an animal drug is not permitted if labeling of another animal drug that contains the same active ingredient and that is in the same dosage form and concentration provides for that intended use.
- If the Secretary finds that an extra-label use of an animal drug may present a risk to the

public health, the Secretary may: (i) establish, either by regulation or order, a safe level for residues of that animal drug and (ii) require development of a practical, analytic method to detect residues above the safe level.

- Use of an animal drug that results in residues exceeding established safe levels shall be considered an unsafe use.
- The Secretary may provide access to the records of veterinarians to ascertain any use or intended use that the Secretary has determined may present a risk to public health.
- The Secretary may, after affording an opportunity for public comment, prohibit an extra-label use of an animal drug if it presents a risk to the public health or if the required analytic method has not been developed.

* *A valid veterinarian/client/patient relationship, as defined by the American Veterinary Medical Association is the following: "An appropriate veterinarian/client/patient relationship will exist when: (1) the veterinarian has assumed the responsibility for making medical judgements regarding the health of the animal(s) and the need for medical treatment, and the client (owner or caretaker) has agreed to follow the instructions of the veterinarian; and when (2) there is sufficient knowledge of the animal(s) by the veterinarian 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), and/or by medically appropriate and timely visits to the premises where the animal(s) are kept; and when (3) the practicing veterinarian is readily available for follow-up in case of adverse reactions or failure of the regimen of therapy."*

Some of the key provisions of Animal Medicinal Drug Clarification Act of 1994 regarding the use of *human drugs* are:

- Extra-label use of FDA approved human drugs will be permitted under the following conditions: (i) by or on the lawful written or oral order of the licensed veterinarian; (ii) within the context of a veterinarian/client/patient relationship; (iii) in compliance with regulations promulgated by the Secretary of Health and Human Services.

Thus, when a veterinarian administers insulin to an insulin-dependent diabetic dog or cat, or administers a cancer fighting drug to a families' companion animal, that veterinarian will no longer be breaking the law as he or she would have been without the Animal Medicinal Drug Clarification Act of 1994 legislation. Similarly, this law assists the veterinarian in that he or she may now, again under FDA regulations, prescribe and/or administer medication to minor species such as sheep, goats, aquatic, and exotic animals even though no approved drug for that specific species or condition may presently exist.

While this extra-label use legislation will be essential to the practicing veterinarian, the overall problem of animal drug availability remains. The Animal Drug Availability Act of 1995 (H.R. 2508), has been introduced in the House of Representatives as has a companion bill, S. 773, in the Senate. This legislation, which is being coordinated with the FDA/CVM, would expedite the animal drug approval process without compromising human health or animal health. Dr. Stephen Sundlof, Director of CVM, is committed to expediting the drug approval process while maintaining current requirements for proving that a product is safe for human health, the food

supply and for the animals. The AVMA supports this legislation and is asking the Congress for its passage.

One of the major problems we hope to see addressed by the Animal Drug Availability Act of 1995 is the excessive time period the CVM is currently taking in deciding whether to approve a new chemical entity for animals. CVM's own study has reported that it can take up to 58 months for the agency to reach a decision. This lengthy time frame and cost are discouraging to the pharmaceutical companies that we rely on to develop new products needed for animal health.

The legislation will incorporate a number of statutory and regulatory reforms that would support the efforts of CVM. Part of the delay in approving new drug applications is tied to overly rigid requirements for demonstrating the effectiveness of new animal drugs. The FD&C Act currently requires efficacy to be demonstrated through "adequate and well-controlled investigations, including field investigation." The FDA has interpreted this language to routinely require three field investigations, each in a different region of the nation. This requirement has led to duplicative tests that are expensive and time-consuming for new drug sponsors but that often yield information of little benefit to the agency, veterinarians and animal drug sponsors. The legislation will amend the statutory definition of what constitutes evidence of effectiveness to allow the FDA to accept one or more scientifically sound studies, including *in vitro* studies, studies in laboratory animals, bioequivalence studies, and any other similar studies, that, taken together, provide reasonable assurance that the drug will have the claimed or intended effect. This is a far more flexible definition, permitting the FDA to adapt the types of studies it requires

to the particular characteristics and proposed uses of the new animal drug. The legislation removes the statutory requirement for "field investigations" but provides the authority to the FDA to require a field investigation when necessary.

Both the FDA and the regulated industry have long struggled with the difficult problems raised by the use of new animal drugs in a minor species or for a minor use. The FDA has recognized that some drugs have extraordinarily small markets because they are either used in a minor species or have very limited use. The FDA has attempted to encourage the development of these drugs by streamlining several of the effectiveness requirements for these drugs. For example, when a manufacturer seeks approval for a use in a minor species of a drug already being used in a major species, the FDA does not always require original effectiveness testing for the minor species use. It allows the sponsor to extrapolate from tests done of the drug in a major species. The provisions in the legislation are consistent with these efforts. The legislation exempts drugs for minor species and uses from the usual requirements for demonstrating substantial evidence of effectiveness if there is a previously-approved animal drug application for the drug.

Further, this legislation will require that FDA provide a new animal drug sponsor an opportunity for a conference prior to the submission of an application, in order to provide advice regarding the requirements that must be satisfied for approval of the product. That advice is binding unless the FDA subsequently determines that a new documented scientific requirement essential to determination of the safety or effectiveness of the drug has appeared after the meeting. Within a reasonable time after any such meeting, if the FDA requires any type of study other than those

specified in the new definition of substantial evidence of effectiveness, the agency must provide a written justification for that requirement, specific to the animal drug and its intended uses. This will assure both that the FDA has the flexibility to require whatever evidence of effectiveness is scientifically justified for a particular drug and its intended uses and that the applicant will receive a full and detailed scientific justification for any unusual requirement, such as a well-controlled field trial.

Another issue of importance to practicing veterinarians and animal owners is one of how best to disseminate drug use information. Because there is not an FDA approval for every drug needed to treat every species for every condition, veterinarians are constantly searching for effective therapeutics to treat the presently untreatable. Extra-label use of drugs is often necessary in those cases where disease conditions are not responding to an FDA-approved treatment or in those cases where no approved drug is available. Cancer chemotherapeutic agents approved for use in humans are effective in many cancers afflicting companion animals but information on dosing regimens for dogs and cats are often not readily available. To better treat our patients it is critical that veterinarians have access to updated information on new uses of products. Oftentimes the best place to go for the most up-to-date information is the drug sponsor and/or veterinary experts in speciality practice. Currently, FDA prohibits the free exchange of information, for example, between veterinarians at sponsored seminars and also between veterinarians and drug sponsors at medical conferences. Veterinarians with expertise who mention extra-label uses in the course of a scientific lecture should be allowed to do so as long as any corporate sponsorship toward this lecture is not extravagant and the sponsor does not control the scientific material presented.

Likewise, industry should be able to distribute information to veterinarians, providing the companies' studies are consistent with the drug being safe and effective, and the studies are peer-reviewed published articles or published reference texts. We would encourage FDA/CVM to come forward with much needed guidelines to allow the dissemination of current, up-to-date information from sponsors to practitioners who are treating the public's animals.

Ladies and gentlemen, the ultimate "raison d'etre" of veterinary medicine is the enhancement of human health as well as animal health. We enhance human health through the prevention of those diseases transmissible between animals and man. We provide pet-owning families with psychological well being through a happy and healthy pet. We safeguard our population's food supply through the prevention and treatment of food borne animal diseases and through our participation in food hygiene and safety inspections. A well staffed and properly resourced Center for Veterinary Medicine is paramount to the successful accomplishment of our mission. I thank you for the opportunity to present these views to the subcommittee and welcome any questions.

AMERICAN VETERINARY MEDICAL ASSOCIATION
1931 N. MEACHAM ROAD, SUITE 100 • SCHAUMBURG, ILLINOIS 60173-4360
PHONE 708-925-8070 FAX 708-925-1329

The Testimony of Sherbyn W. Ostrich, V.M.D.

The American Veterinary Medical Association, representing 58,000 doctors of veterinary medicine, is very much aware of the awesome responsibility that is placed upon us in protecting the public health, including the proper and professional administration of therapeutic drugs to food animals. Because veterinarians are professionally trained to be knowledgeable in comparative pharmacology, pathology, bacteriology, virology, parasitology and epidemiology, we strongly feel that prescription labeled drugs should only be administered by or under the supervision of a licensed and accredited veterinarian.

We strongly feel that any decision on the use of any class or specific antibiotic in animals should be a science based decision; i.e., those decisions should not be based on supposition or innuendoes. We will work categorically in cooperation with CVM/FDA to protect the nation's food supply from harmful residues of any source and will help to see that violators are dealt with to the full extent of the law.

We ask only that the recently passed extra-label modification of the medicinal Drug Act of October 1994 be allowed to work in the spirit of its intention.

This committee should be comforted to know the veterinarian's oath says that veterinarians "solemnly swear to use their (sic) scientific knowledge and skills for the benefit of society through the protection of animal health, the relief of animal suffering, the conservation of livestock resources, the promotion of public heath, and the advancement of medical knowledge." In other words, the public's health is our business!

5/6/96-dmv--SWOTEST

Mr. SHAYS. Thank you very much. What we're going to do is we're going to recess. And we're going to try to get back as soon as we can. I think we only have one vote. Then, Dr. Wolf, we'll hear you. We're going to try to finish up about 15 after if we can, but we'll see. Thank you.

[Recess.]

Mr. SHAYS. The hearing will come to order. Dr. Wolf, we're going to hear from you. By the way, I thank the third panel. The third panel has to sit through the entire first two, but we appreciate, one, that you came; and, two, that you are patient and willing to go through the other panels.

Dr. WOLF. My name is Cindy Wolf. And I am here today on behalf of the American Sheep Industry Association. And we thank this committee and the chairman for the opportunity to come speak with them.

I work at the College of Veterinary Medicine at the University of Minnesota in the capacity as a small ruminant specialist, which means that I teach veterinary students, provide veterinary care to small ruminants and provide outreach which formally was extension to veterinary practitioners and producers. I also chair the Sheep Health and Welfare Committee of the American Sheep Industry Association; am a board member of the American Association of Small Ruminant Practitioners; am a member of the AVMA; and am also a commercial sheep producer.

Providing adequate health care for sheep can be a problem. There are currently 21 pharmaceutical products labeled for sheep. There have been very few new product approvals in the last several years. And we are currently in desperate need of labeled products to treat respiratory illness.

Another example of a current need and an important one, I might add, is estrus synchronization products. The American Sheep Industry Association, or ASI, is presently conducting an industry wide survey in cooperation with USDA APHIS to ascertain health and productivity problems. This survey will provide a current data base, which industry and Government can use to prioritize products and health program needs.

Historically, sheep have been classified as a major species. In 1990 and three times since, ASI has requested that FDA/CVM reclassify sheep as a minor species. We believe this reclassification is entirely justified based on some statistics provided year after year by the USDA.

On January 1, 1996, USDA's inventory report that there are approximately 9 million sheep in the United States, and this includes 5.5 million breeding animals. The consumption of sheep meat nationwide is less than 1 pound per capita of boned and trimmed product weight. However, there are areas of higher per capita consumption such as the Baltimore to Boston corridor, which comprises about 45 percent of national consumption and an average of 3 pounds consumed per capita.

Recently, CVM has administratively designated sheep as a minor species. We appreciate this administrative designation. However, we would urge that designation be published formally. And I might point out that there are seven major species recognized by the

FDA/CVM. And they are cattle, swine, horses, dogs, cats, chickens, and turkeys.

I would like to thank FDA/CVM Director, Dr. Sundlof and his staff for entering into an open dialog with us over the past couple of years on the drug approval issue and their willingness to try and help find solutions to some of our serious problems. Currently, extra label use is essential for proper flock health programs, sheep flock health programs.

Though we cannot effectively do without extra label use today, there are problems associated with it. Because of the lack of available specific information for our species and our need to adhere to the FDA compliance guidelines, veterinarians are often reluctant to use extra label products to treat sheep. Neither veterinarians or producers have good information on withdrawal times or dosages for these extra label products. We as small ruminant practitioners and sheep producers are very concerned about food safety and ensuring the quality of our products.

ASI has invested significant resources to develop a comprehensive quality assurance program. This program encourages both veterinarians and sheep producers to be cautious and responsible about product use.

And I would like to enter for the record a publication about our quality assurance program.

If a product is used extra label, the liability falls on the veterinarian and the producer. If a product is labeled for a specific use in a specific species, then the manufacturer shares in the liability. But the acceptance of this liability or the pursuit of this liability on behalf of the manufacturer must be worthwhile in order for them to make the substantial investments required in seeking FDA label approval.

We believe that statutory changes are necessary so that incentives can exist for manufacturers to make available the much needed new health products for sheep. Legislation is pending before Congress that could address some of our concerns. The animal drug availability and title 2 of the FDA reform bill would be a giant step forward in modernizing the drug availability process. And we thank the members of this committee for their sponsorship of H.R. 3200.

In particular, it should include provisions for minor species designation, though I understand that inclusion of the minor species minor use provisions in the legislation may be in question by the FDA, the issue must be addressed, either in this legislation or separately in a more comprehensive manner if we are serious about effecting substantive change.

I believe that in evaluating products for safety and efficacy, scientifically sound data from anywhere in the world should be used. I understand that there is a trend within the FDA/CVM to now give more attention to sound foreign data. I believe that this is a very positive step and should be encouraged. Many pharmaceuticals have been developed, tested, and are marketed in major sheep producing countries, such as New Zealand and Australia. These tools, if available in the United States, would give veterinarians and producers the opportunity to improve flock health.

The National Research Support Project No. 7, which we'll call NRSP No. 7, is a project that is largely funded by USDA, partially managed by FDA, and designed to expedite drug approvals for minor species. It has been key in the sheep drug approval process. And though a tremendous amount of progress through the program is now being made, it is extremely underfunded and understaffed. And I might add that there is only one person in the FDA who works on this program. And as far as minor species that she looks after under that program, it's not limited to sheep. It's limited to minor species of agricultural importance.

In summary, I would like to emphasize the following points. Statutory changes and perhaps regulatory reform are needed in drug availability, including minor species, minor use to both modernize and expedite the drug approval process, as well as to assure food safety. Methods should be developed, which provide incentives for manufacturers to label products for minor species use. Sheep need to be formally reclassified by FDA as a minor species. And the NRSP 7 program needs additional support in the way of personnel and funding.

And if you would permit me, Mr. Chairman, I would like to make a few comments relative to the sheep industry and the BSE discussion, if I could.

First, we would like to applaud the National Cattlemen's Beef Association in their initiative to endorse a voluntary ruminant-to-ruminant protein feed ban. We would like everyone to know that, since 1989, there has been a voluntary ban on rendering sheep in place. And it has been working quite well.

We are urging the FDA in their proposed rulemaking to include deer and elk in their ruminant-to-ruminant protein feed ban.

And, last, we would just like to go on record saying that it is still in question scientifically regarding what is the original source of BSE in the United Kingdom. And at the moment, it is still not proven that sheep were the original source.

Thank you very much.

[The prepared statement of Dr. Wolf follows:]

My name is Cindy Wolf. I am Assistant Professor in Clinical and Population Sciences in the College of Veterinary Medicine at the University of Minnesota. My capacity there is Small Ruminant Specialist which includes teaching veterinary students, administrating flock and herd health programs, including clinical care at the college and on Minnesota farms, as well as outreach (extension) to veterinary practioners and producers. I am also Chair of the Animal Health and Welfare Committee of the American Sheep Industry Association (ASI), a board member of the American Association of Small Ruminant Practitioners, and a sheep producer.

Providing adequate health care for sheep can be a problem. There are currently fewer than 20 pharmaceutical products labeled for sheep. There have been three product approvals in the last three years. We are currently in desperate need of label products to treat respiratory illness. Another example of a current need is estrus synchronization products. ASI is conducting an industry-wide survey in cooperation with USDA/APHIS designed to ascertain health and productivity problems. This survey will provide a data base which industry and government can use to prioritize product and health program needs.

Historically sheep have been classified as a major species. In 1990 and three times since, ASI has requested that FDA/CVM reclassify sheep as a minor species. We believe this reclassification is entirely justified. According to USDA's January 1, 1996 inventory report, there are approximately 9 million sheep in the United States. This includes approximately 5.5 million breeding animals. The consumption of sheep meat nationwide is about 1.3 pounds (carcass weight) per capita which translates to less than one pound per capita (boned and trimmed product weight). However, there are areas of higher per capita

consumption, such as the Baltimore to Boston corridor, which comprises about 45 percent of national consumption at an average of 3 pounds consumed per capita. Recently, CVM has administratively designated sheep as a minor species. We appreciate this administrative designation; however, we would urge that the designation be published be formally.

I would like to thank FDA/CVM Director, Dr. Sunlof, and his staff for entering into an open dialogue with us over the past couple of years on the drug approval issue and their willingness to try and help find solutions to some of our serious problems. Currently, extra label use is essential for proper flock health programs. Though we cannot effectively do without extra label use today, there are problems associated with it. Because of the lack of available specific information and our need to adhere to the FDA Compliance Guidelines, veterinarians are often reluctant to use extra-label products to treat sheep. Neither veterinarians or producers have good information on withdrawal times, dosage, and usage on these extra-label products. We, as small ruminant practitioners and sheep producers, are very concerned about food safety and assuring the quality of our products. ASI has invested significant resources to develop a comprehensive quality assurance program. This program encourages both veterinarians and sheep producers to be cautious and responsible about product use including extensive records.

If a product is used extra-label, the liability falls on the veterinarian an the producer. If a product is labeled for specific use, then the manufacturer share in the liability. The acceptance of this liability on behalf of the manufacturer must be worthwhile, in order for them to make the substantial investments required in seeking FDA label approval. We

believe that statutory changes are necessary so that incentives can exist for manufacturers to make available the much needed new animal health products for sheep.

Legislation is pending before Congress that could address some of our concerns. The "Animal Drug Availability" provisions of HR2508 and title two of the FDA Reform Bill, HR3200 would be a giant step forward in modernizing the drug availability process. In particular, it should include provisions for minor species designation. Though I understand that inclusion of the minor use/minor species provisions in the legislation may be in question by the FDA, the issue must be addressed, either in this legislation or separately in a more comprehensive manner, if we are serious about affecting substantive change.

I believe that in the evaluating products for safety and efficacy, scientifically-sound data from anywhere in the world should be used. We also need to find a way to make these data available to the veterinary profession to guide their administration of extra-label use products. I understand there is a trend in FDA/CVM to now give more attention to sound foreign data. I believe this is very positive step and should be encouraged. Many pharmaceuticals have been developed, tested, and are marketed in major sheep producing countries, such as New Zealand and Austria. These tools, if available in the U.S., would give veterinarians and producers the opportunity to improve flock health.

The National Research Support Project-7 (NRSP-7) is largely funded by the USDA, managed by FDA, and designed to expedite drug approvals. It has been key in the sheep drug approval process though a tremendous amount of progress through the program is now being made, it is extremely under funded and under-staffed.

In summary I would like to emphasize the following points.

- Statutory changes and perhaps regulatory reform are needed in drug availability, including minor species/minor use to both modernize and expedite the approval process, as well as to assure food safety.
- Methods should be developed which provide incentives for manufactures to label products for minor species' use.
- Sheep need to be formally reclassified by FDA as a minor species.
- NRSP 7 program needs additional support (personnel and funding).

I appreciate the Subcommittee's consideration of this important animal health issue for the U.S. sheep industry.

Mr. SHAYS. Thank you. I'm going to call Mr. Towns first, but I'm just curious on two issues just so I have a perspective. The quantity of sheep compared to the number of cattle is quite small. Are sheep concentrated in certain areas of the country?

Dr. WOLF. Texas and California would be the No. 1 and No. 2 sheep-producing States respectively. But there are sheep distributed throughout the country.

Mr. SHAYS. When I was overseas, I was on an island near New Zealand. New Zealand had a tremendous quantity of sheep. What makes New Zealand a sheep country and the United States not? Is it just historic or is it just an economic issue?

Dr. WOLF. It is somewhat based on tradition. You can see the grass grow in New Zealand and that's a tremendous resource they have to economically raise sheep. We also have a misperception in this country that grazing ruminants are bad. And we could afford to graze many more ruminants, including sheep, in areas of the country that we do not at present.

Many livestock producers think they don't want to raise sheep because historically they require more work than raising cattle. That's not necessarily the case. We have 82,000 people raising sheep in this country at the moment.

Mr. SHAYS. Thank you. How often do you get teased about being Dr. Wolf and taking care of sheep?

Dr. WOLF. Well, you know people are listening when that happens.

Mr. SHAYS. Does it happen often? I'm sorry.

Dr. WOLF. That's OK.

Mr. SHAYS. I knew it happened often and I still had to bring it up. Mr. Towns.

Mr. TOWNS. I think they might deal with Dr. Ostrich a little bit, too.

Dr. OSTRICH. All of the time.

Mr. TOWNS. Thank you very much, Mr. Chairman. Dr. Welser, I appreciate your comments. The decision about food safety and approval of veterinary products should not be made because of media hype or hypothetical fears, you indicated. Have you seen any evidence of Congress or the FDA being pressured to act too hastily?

Dr. WELSER. No, not in my experience base have they acted hastily in terms of the approval process. I think you are seeing this on the human pharmaceutical side with the AIDS and cancer drugs resulting in an expedited review system. That does not occur in the animal side in terms of animal pharmaceuticals. But in the human side now with AIDS and cancer, there has been expedited reviews.

Mr. TOWNS. How about you, Dr. Ostrich?

Dr. OSTRICH. No, I haven't. Because in companion animal medicine, nobody really cared too much as long as we made their animal well with what drugs we used. And we've always had the ability to write a prescription for drugs that we did not have on our shelf, and they could go to the pharmacy and pick the human drug up and use it.

But we were really acting outside of the law, but everybody always looked the other way. Now, with this new bill, of course, we're acting within the law.

Mr. TOWNS. Dr. Wolf.

Dr. WOLF. No, I have not.

Mr. TOWNS. Thank you. Dr. Welser, you testified that a problem with the phase review system is coordination at the final approval stage. Please describe how this problem is currently affecting you.

Dr. WELSER. Well, what happens is as you're submitting applications in phases, you may get your environmental impact and your efficacy approved in one package. You may get your chemistry and manufacturing approved in another. And then you get your path-tox section in another.

When the approval is completed on each of them, theoretically it should all come together and one letter goes out. But what happens is, in the final review as it goes through the FOI process, one group will say, I can't believe that you approved that compound through the path-tox system.

The path-tox people say, yes, we did because of the data that was presented.

Or the efficacy people will say, that is not the same product that was used in the pre-clinical trials that was used in the final efficacy trials. And there is the re-review of the section. Dr. Sundlof is very aware of this and has brought persons together and said, we will go in a room now and have a post-approval or a pre-approval package discussion.

So the result was this last one where we got it out in 2 weeks. That was the product of having each of those facets approved and then all going into a room and saying, OK. Let's coordinate the final review and get it done.

So I think that is going to be cleared up.

Mr. TOWNS. Dr. Ostrich, basically has your organization experienced problems with coordination in the phase review process?

Dr. OSTRICH. Yes. What I stated before, the fact that all of these drugs have been tested in animals—now, not necessarily food producing animals. That's a different story altogether. In food-producing animals we need further testing to see how rapidly those drugs leave that animal system, so we can advise the farmer when that animal can go to market safely.

But in companion animals, to us, it's always seemed pretty ludicrous that they would have to retest these drugs in the animals to get a label for dogs and cats.

Mr. TOWNS. Dr. Wolf.

Dr. WOLF. What we've seen is, because of what is getting close to be called understaffing within FDA, it is happening that there is a backlog of review. And people within the FDA will acknowledge that or at least have to me. And because of that, there have been delays.

The other issue in delays for us from a minor species desirability standpoint is the consideration of foreign data. That's a relatively new concept and not fully employed by the FDA. And we'd like to see that be utilized more, where in countries where they're in excess of 40 million sheep, they do have some drugs available that we would like to have and need in this country. And the data does exist. So there is not a need to redo the work if it satisfies FDA review if they'll look at the data.

Mr. TOWNS. Right. I think one of you indicated that the delays cost your company like $25 million for every year. Today it was

stated, $25 million for every year that a drug approval was delayed. Someone made that comment here today.

Dr. WELSER. Dr. Sundlof made the statement that a drug entity for animals takes 10 years and approximately $25 million to be brought to the market. And I would agree with that term.

As to what it costs per year in a delay, that is related to the ultimate market value of the drug. So it's very easy, if you're talking about a $30 million potential drug or a $10 million potential drug to add up what that daily revenue might be for each day that it is delayed.

Mr. TOWNS. I was aware of the fact that I heard that somewhere today.

Dr. WELSER. You're correct.

Mr. TOWNS. I must admit I got up really early this morning, but it was today.

Dr. WELSER. Right.

Mr. TOWNS. A comment was made by Dr. Sundlof, I think, in terms of that. So let me just sort of follow up on that by asking all of you—I think one has already commented on it already. What is your impression of the work that Dr. Sundlof has done since becoming Director of CVM?

Mr. SHAYS. Normally, you don't have to deal with him at all after you answer this question.

Mr. TOWNS. If you want to make no comment on it, I'll accept that on this one.

Dr. OSTRICH. I would give him high marks because he is trying to improve the process. In that position, a lot of times you're between a rock and a hard place because you have to make consumers happy and you have to make producers happy. And you have to make the veterinarians happy. It's a tough box to be in. But I think he's at least made progress already in his short term in office.

Mr. TOWNS. I'll go to you, Dr. Welser, because Dr. Wolf sort of indicated you, so.

Dr. WELSER. Dr. Sundlof, in my book, has done a lot in his short period of time as the head of the Center. And I would echo what Dr. Ostrich said here. But specifically he has taken a hard look at the efficacy requirements, while not de-emphasizing human food safety and target animal safety and the environment, which are the key areas in terms of protecting the public and the animal owner.

And he has instituted things like team building. I know he's taken the staff off on retreats. He's produced a strategic plan. That's where my quote came about what surveillance and compliance was directing its efforts to, which permits us then as customers to say, wait a minute, I think you're directing your efforts in the wrong way. So it provides an opportunity for comment, et cetera.

So I would give him very high marks.

Mr. TOWNS. Do you want to add some other things, Dr. Wolf?

Dr. WOLF. No.

Mr. TOWNS. So, in other words, if we can get him the resources, we might have something going?

Dr. WELSER. Yes.

Dr. OSTRICH. Right.

Dr. WOLF. Yes.

Mr. TOWNS. I want to say that where the chairman can hear it. The comment was made by someone that if he could get some additional resources, we might have something going with him. That was the comment. I yield back.

Mr. SHAYS. I would like to just have you describe to me, Dr. Ostrich, you basically focused on companion animals. Why is that?

Dr. OSTRICH. Well, basically, that's what I was told to do.

Mr. SHAYS. That's the reason. I need to know that. But it is basically because of our request and not just because you felt that it needed a particular area? I want to know if this was your expertise area or whether you focussed on both sides of this issue.

Dr. OSTRICH. Well, like I said, I was in food animal practice for 10 years before I went all companion animals.

Mr. SHAYS. I just want to know the answer. I'm happy you did. I just want to know what your motivation was.

Dr. OSTRICH. My motivation was basically that's what I was asked to address.

Mr. SHAYS. Give me the distinction between our dealing with companion animals versus, what, food animals?

Dr. OSTRICH. Yes.

Mr. SHAYS. How should I view these two different—I might say parenthetically that when I was first—I'm interrupting you. I'm sorry. When I was elected in the special election in 1987, I got more letters from animal rights advocates than contra aid funding. It was the biggest number of letters on any issues that I received in my first 2 years. It's an amazing thing. There's a network of very concerned people about animals obviously.

But bottom line. How do I view the difference?

Dr. OSTRICH. The difference is food safety. And food safety, of course, is large in the headlines today. And on the other hand, the issue that companion animals stay healthy is extremely important because there is mounting evidence that pets keep people healthy.

Mr. SHAYS. But I was wondering should we have the same standard of purity in the sense of regulation over companion animals as we have over food animals, or we have over human beings in terms of wanting to protect the patients?

Dr. OSTRICH. As far as the efficacy of the drug?

Mr. SHAYS. Yes.

Dr. OSTRICH. Definitely.

Mr. SHAYS. I'm sorry. I didn't hear you.

Dr. OSTRICH. Yes. I'll give you an emphatic yes. We should have the same.

Mr. SHAYS. Describe to me why just for the record.

Dr. OSTRICH. Well, simply because I, as a doctor of veterinary medicine, would be uncomfortable using a drug that I felt may not have the purity and the standards for that patient and that would be best for that patient.

I'll give you an example. There was a proposal to let up on standards for an anesthetic, a local anesthetic coming off the production line as far as the final sterilization process of that product. And if they didn't have to sterilize it once more as is in the regulations,

it would save the x number of dollars of putting that drug out in the market.

We voted emphatically as a board not to approve that.

Mr. SHAYS. What I was driving at—and I can see your answer. And I agree with it. I understand if you're in your profession, you would want to only use what you knew would do the job. But I'm really kind of getting the whole concept. And that's why I was trying to be refreshed, the concept of the Delaney clause. I mean, there are some of us—and I think myself included—that feel that the Delaney clause has been used almost to an absurdity in terms of public safety for human beings. So, I mean, it's an incredibly tough standard.

Dr. OSTRICH. Especially in light of the technology today.

Mr. SHAYS. Right. So my instinct is saying if you were going to drop it anywhere, you would start maybe with companion animals.

Dr. OSTRICH. Well, I don't even know that we would ever measure the amount of residue left in a companion animal. We would have no reason to.

Mr. SHAYS. The question is: So the standard is quite different for humans?

Dr. OSTRICH. In that respect, absolutely, yes, sir.

Mr. SHAYS. Is the standard for companion animals and food animals—do we have the same kind of concept with the Delaney test? I'm asking the question that maybe almost everyone else knows, but I don't, so I'm going to ask it.

Let me just be very clear. Do we have the same kind of standard test for companion animals—first, let me ask this. Food animals and companion animals have the same basic test? It has to meet the same standard? We don't distinguish between the two?

Dr. OSTRICH. The drugs? You mean the drugs?

Mr. SHAYS. The drugs supplied to either. Do we have a higher standard for food animals than we have for companion animals?

Dr. OSTRICH. Yes, right now.

Mr. SHAYS. And we have a higher standard for human beings as we do to food animals?

Dr. OSTRICH. Not really. I don't think so.

Dr. WELSER. That one would be tough to really delineate between whether there is a higher standard for human drugs than there are for——

Mr. SHAYS. Do we have the Delaney test for food animals?

Dr. WELSER [continuing]. Yes. Food animals, the primary difference between food animal and the companion animal are the requirements for long term carcinogenic studies, development of a drug residue method and development of a drug withdrawal time which requires that you do in-depth metabolism work. For a companion animal, though, you do have to have drug curves as to how long it lasts, what the metabolism rate is, what's the ultimate deposition. Because that comes into your environmental impact statement that you have to file with it.

Mr. SHAYS. Was it your testimony, Dr. Ostrich, that tests for humans—I mean, for our market, that there are some drugs that would be used on animals quite similar or identical?

Dr. OSTRICH. Absolutely.

Mr. SHAYS. The answer is yes?

Dr. OSTRICH. Yes.

Mr. SHAYS. Then if it was safe for—what do you do differently for animals that—is there a different test that you have to do?

Dr. OSTRICH. Let me explain it to you this way.

Mr. SHAYS. I mean, this strikes me as very funny, when you think about it.

Dr. OSTRICH. Different species metabolize drugs at a different rates. So the rate it leaves the animal system may be different. But the effects of the drug are probably the same.

So when we take a human label drug and put it in other species, we have to determine what is the most efficient level and how much to give over a period of time.

Mr. SHAYS. But the difference in testing drugs for animals is you can actually take the animal and test it on the animal that eventually you want to sell in the open market where you're not going to test with human beings.

Dr. OSTRICH. Right. But with food animals, as was pointed out, it's very important to know how much residue will be left in that animal after x number of days. And that's where we differ in companion animals and food animals.

Mr. SHAYS. Dr. Wolf, do you want to jump in on this? I'm sorry. I didn't know if you would like to comment on any of the questions I asked.

Dr. WOLF. It's a good question, because we do make the assumption.

Mr. SHAYS. I needed that reinforcement. Thank you. I feel my staff tightening up when I ask some of these questions. My God, we told him the difference.

Dr. WOLF. For instance, as you go from—just pick a horse for a moment or pick a food animal. You go from an adult to a neonate. The metabolism is so different that, even though we may know the dose for the adult, the dose would be inappropriate for the neonate. And you can basically destroy kidneys in a matter of 24 hours using an adult dose in a neonate. So it's an important issue.

Mr. SHAYS. What types of animal drugs are needed? Antibiotics, disease specified therapies, or hormones? Are there particular drugs more needed than other drugs?

Dr. WOLF. The animals almost display the same number of diseases as humans display. And there may be some species differences in that a dog may get one type of bacteria, but a man may not. But it's one medicine. It's just comparative.

Mr. SHAYS. This may be a crazy way to state it, but is there potentially big money in pharmaceuticals for animals; or is it just very limited? Does the market place not work as well in this industry as it would, say, with humans?

Dr. OSTRICH. Not near as high.

Mr. SHAYS. Pardon me?

Dr. OSTRICH. The market is not near as lucrative in animals as it is in humans.

Dr. WELSER. In the food animal industry, before a drug can penetrate the market, you really have to have cost benefit. So it is cost driven in addition to the approval process.

Mr. SHAYS. Well, it has to be.

Dr. WELSER. Right, or it's not going to make a market. There are only two drugs that I'm aware of that are over 100 million currently in the market. One is called Program, which is a flea insecticide. And the other one is Ivermectin, which is made by Merck Co. which is a very effective parasiticide.

The economics of the industry are not that great currently, as I am aware, of the 22 companies that are active in the animal health business in the United States today, members of HHI, only 5 are developing new clinical entities. The rest are maintaining and preserving their current product line.

Extra label drug use, quite honestly, in the companion animal precludes many of the companies from entering that market or developing a product for that market because of the availability of human generics and the widespread use of them.

Mr. SHAYS. One last question. How concerned should we be about the antibiotic residues in meat as a factor in antibiotic resistancy?

Dr. OSTRICH. I'll take a crack at that answer. There is very little, if any, substantiated scientific evidence that antibiotic use in animals produces organisms that will affect humans and be resistant because of the antibiotic use in animals. There has always been innuendo and possibilities, but nothing has ever been really substantiated in a way that we can embrace it as, that's scientific evidence.

Mr. SHAYS. I have to catch an airplane. I don't know if Mr. Towns does, as well. But your knowing that, do you have anything that you want to just kind of conclude with? Is there any point that you wished we had asked? Anything that you want the committee to know. And I'm serious. If there is something you want on the record, I'd like you to put it on the record. Is there any comment, Dr. Wolf, that you'd like to make?

Dr. WOLF. No, thank you.

Dr. OSTRICH. Only that I don't know how much influence the committee will have on allowing CVM to accept the data that's been used producing human drug for use in animals.

Mr. SHAYS. I just love the concept, so I think we're going to pursue that.

Dr. WELSER. The other thing is, encourage harmonization between the major regulatory agencies of the world. Going back to her point, Japan, Europe, Australian, the United States, and Canada are the major countries that have regulations. They're not in harmony.

Mr. SHAYS. Is that something that we should devote a hearing to? Is that an issue that we should invite?

Dr. WELSER. I think it is an issue that should be dealt with. It's not certainly as timely as BSE.

Mr. SHAYS. But it is interesting, because the World Health Organization came up in our hearings in a way that was different than some of our other hearings. I thank all of you for participating. I'm very grateful that such distinguished people have addressed this committee today. And we appreciate how you have honored our committee and helped us.

I'd like to thank Patricia Kueber, our reporter, for helping us out today; and Tom Costa, our clerk, who I never recognize but who has always been so helpful; and Marcia Steinberg, who is our legislative fellow from National Science Foundation. Marcia, we appre-

ciate it. And Anne Marie Finley, who is our expert on our committee and is a real find for our committee staff. And I appreciate obviously my staff director and Cheryl Phelps, who has been very helpful. And this guy sometimes has been good, too. So I appreciate Larry Halloran as our staff director, and all of you for coming. Thank you. I'm going to have to rush off.

[Whereupon, at 2:25 p.m., the subcommittee was adjourned.]

[Additional information submitted for the hearing record follows:]

Cardiss Collins, M.C.

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OPENING STATEMENT OF THE HON. CARDISS COLLINS
SUBCOMMITTEE ON HUMAN RESOURCES AND
INTERGOVERNMENTAL RELATIONS

"Food safety: oversight of the Food and Drug Administration's Center for Veterinary Medicine"

May 10, 1996

Mr. Chairman, I am pleased to join you and the ranking Member of the Subcommittee, Rep. Towns, to consider the operations and priorities of the FDA's Center for Veterinary Medicine. The mission of this FDA unit is an integral part of the Federal government's efforts to ensure the safety and integrity of our nation's food supply.

CVM's regulatory oversight of the veterinary medicines and feeds that maintain the health of food-producing animals is our first line of defense against disease-causing micro-organisms such as salmonella and E. coli bacteria.

Through the valuable work of the FDA, other Federal agencies such as the Department of Agriculture, and the commitment and cooperation of the food industries, the U.S. food supply is the safest in the world. But despite this hallmark, GAO estimates of number of cases of food-borne illness reaches as high as 80 million each year; and most experts believe that the numbers will escalate in the future.

Chairman Shays, I commend your leadership and vision in seeking to assess the ability of the Center for Veterinary Medicine to carry out its current mandate. I imagine also, that the Subcommittee's oversight will help us determine whether the Food and Drug Administration and other Federal agencies are positioned to respond to the public health crisis that may be looming on the horizon.

But let's not be disingenuous about our interest in solving this problem. Last year, the Republican majority orchestrated serious and very nearly successful attempts to kill the Department of Agriculture's new meat and poultry inspection rule. This act was first attempted under the guise of a moratorium on rulemaking. Another attempt to kill the rule occurred during the appropriations process. That effort would have succeeded but for the intervention of the Secretary of Agriculture.

Now that the rule is in its final stages, concerns have been raised that, due to outside pressures, the final rule may not require microbial testing of meat and poultry.

Mr. Chairman, this is outrageous. Any failure to incorporate microbial testing into the Agriculture Department's Hazard Analysis and Critical Control Point inspection system is like handing the American public a gun with one bullet in the chamber and saying "pull the trigger before every meal".

Without the appropriate safeguards, consumers are completely defenseless against microbial contaminants in animal products. Yes, it is crucial that the Center for Veterinary Medicines exercise the greatest possible and most expeditious vigilance of new animal drugs and feeds; but it is equally important that CVM's efforts are buttressed by sound inspection techniques that include microbial testing. If CVM is the first line of defense, then I would say that a comprehensive USDA inspection program is the rear guard.

Last week, six of my colleagues and I wrote a letter to the Secretary of Agriculture urging that microbial testing be made a part of the USDA's meat and poultry inspection program. I have included a copy of this letter with my written statement to be entered in the hearing record.

Chairman Shays, I encourage you and other Subcommittee Members who agree with me that all appropriate safeguards -- from a capable and effective Center for Veterinary Medicine, to strong inspection rules -- must be exercised, communicate directly to the Secretary that the USDA final rule be issued as soon as possible, and that it also retain the microbial testing provision.

Congress of the United States

Washington, DC 20515

May 3, 1996

The Honorable Dan Glickman
Secretary of Agriculture
Fourteenth Street and Independence Avenue, SW
Washington, D. C. 20250

Dear Mr. Secretary:

We understand that the Department's new meat and poultry inspection rule is in the final stages of the rulemaking process. We applaud you for your strong and sustained commitment to issuing this rule as soon as possible. There has not been a comprehensive revision of USDA's meat and poultry inspection rules since 1906, and the public is demanding the greater protection that can only be provided by a complete overhaul of this outmoded system.

The final rule must provide for microbial testing of meat and poultry. Ten years ago, the National Academy of Sciences first recommended that microbial testing be made a part of USDA's meat and poultry inspection program. As you know, concern over bacteria in meat is, in large part, the reason a new meat inspection rule was originally proposed.

In recent years, we have seen numerous fatal outbreaks of food-borne illness caused by bacterial contamination of meat. The public now fully understands that only microbial testing can detect deadly bacteria in meat and poultry, and thus save lives.

It is time now to give Americans the protection they want and deserve. Microbial testing is the cornerstone of improved meat and poultry inspection to protect the lives of consumers.

Sincerely,

Cardiss Collins

CARDISS COLLINS
Member of Congress

George E. Brown, Jr., M. C.

Louise Slaughter, M. C.

Charles Schumer, M. C.

Robert G. Torricelli M. C.

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Nita Lowey, M. C.

Dick Durbin, M. C.

3

M.S.. Collins
Durbin
Torricelli
Slaughter
Schumer
George Brown
etc.

STATEMENT BY
THE AMERICAN FARM BUREAU FEDERATION
TO
COMMITTEE ON GOVERNMENT REFORM AND OVERSIGHT
SUBCOMMITTEE ON HUMAN RESOURCES AND
INTERGOVERNMENTAL RELATIONS
REGARDING
"FOOD SAFETY: OVERSIGHT OF THE FOOD & DRUG ADMINISTRATION'S CENTER FOR VETERINARY MEDICINE"

May 10, 1996

The American Farm Bureau Federation represents over 4.5 million families, from all 50 states and Puerto Rico. Our membership includes the majority of the livestock producers in the nation. We appreciate the opportunity to provide comments relative to the Center for Veterinary Medicine.

We are fortunate in the United States to have the most plentiful, affordable and safest food supply in the world. This does not come by accident, but rather is the result of cooperative efforts between producers, processors, retailers, and state and federal regulators. We want to assure that this system continues to provide consumers with the safe food supply that they want and deserve. In this regard, we would like to share our thoughts with you on two issues of concern to the subcommittee.

Bovine Spongiform Encephalopathy (BSE) has had substantial coverage by international media in recent weeks. While there has been a great deal of discussion about the disease, much is still unknown about it. Ongoing research will provide us with more answers in the relatively near future.

We are fortunate that we do not have BSE in the United States. AFBF supports efforts to provide consumers with assurances that proper precautions are being taken to prevent it from occurring in the future.

The following proactive steps are worth noting:

- Banning the importation of live ruminants and ruminant products from countries where BSE is known to exist since 1989;
- Surveillance and post-mortem examination of brain tissue from animals with neurological problems;
- Tracing and surveillance of animals imported from Great Britain prior to 1989; and
- A voluntary ban on the use of rendered products from adult sheep in animal feeds since 1991.

These actions have provided assurance that we do not have BSE in the country. The livestock

industry, has voluntarily stopped the feeding of ruminant derived protein back to animals, providing one more step to assure the public of the continued safety of our food supply as we learn more of this disease.

The Center for Veterinary Medicine (CVM) of the Food and Drug Administration (FDA) is actively involved with USDA and the industry in working groups to address all aspects of BSE. To assure that the best available science is used in all decision making, we strongly encourage this ongoing effort.

Current industry initiatives, which were previously noted, provide extra safeguards for our system. This should allow FDA adequate time to review all pertinent research relative to BSE, and determine if any additional regulatory action is needed. Any decision will be based on sound science. We endorse this approach.

Another issue of concern to the livestock industry has been the lack of availability of new animal health products. All species currently have limited numbers of products available for the treatment of disease. The extended time periods required in the approval process in recent years has been a concern for producers and veterinarians as well as the pharmaceutical industry. We are pleased with recent efforts by CVM to speed the process without sacrificing safeguards for human or animal health. This should improve the situation. We support responsible reform of the process, such as that included in Title VIII of S. 1477.

We appreciate the opportunity to share these thoughts with the subcommittee. We encourage you to support FDA in moving forward with a reasoned approach, based on science, to address both the BSE issue and that of animal health product availability.

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