ANTIBODIES IN ANIMAL HEALTH MAINTENANCE

HEARING

BEFORE THE

SUBCOMMITTEE ON DAIRY AND POULTRY

OF THE

COMMITTEE ON AGRICULTURE

HOUSE OF REPRESENTATIVES

NINETY-FIFTH CONGRESS

SECOND SESSION

SEPTEMBER 27, 1978

Serial No. 95-SSS

Printed for the use of the Committee on Agriculture

U.S. GOVERNMENT PRINTING OFFICE
35-830 O WASHINGTON : 1978

COMMITTEE ON AGRICULTURE

THOMAS S. FOLEY, Washington, *Chairman*

W. R. POAGE, Texas,
Vice Chairman
E DE LA GARZA, Texas
WALTER B. JONES, North Carolina
ED JONES, Tennessee
DAWSON MATHIS, Georgia
GEORGE E. BROWN, JR., California
DAVID R. BOWEN, Mississippi
CHARLES ROSE, North Carolina
JOHN BRECKINRIDGE, Kentucky
FREDERICK W. RICHMOND, New York
RICHARD NOLAN, Minnesota
JAMES WEAVER, Oregon
ALVIN BALDUS, Wisconsin
JOHN KREBS, California
TOM HARKIN, Iowa
JACK HIGHTOWER, Texas
BERKLEY BEDELL, Iowa
GLENN ENGLISH, Oklahoma
FLOYD J. FITHIAN, Indiana
JOHN W. JENRETTE, JR., South Carolina
RAY THORNTON, Arkansas
LEON E. PANETTA, California
IKE SKELTON, Missouri
JOSEPH S. AMMERMAN, Pennsylvania
JERRY HUCKABY, Louisiana
DAN GLICKMAN, Kansas
DANIEL K. AKAKA, Hawaii
HAROLD V. VOLKMER, Missouri
CHARLES WHITLEY, North Carolina
TED RISENHOOVER, Oklahoma

WILLIAM C. WAMPLER, Virginia,
Ranking Minority Member
KEITH G. SEBELIUS, Kansas
PAUL FINDLEY, Illinois
CHARLES THONE, Nebraska
STEVEN D. SYMMS, Idaho
JAMES P. JOHNSON, Colorado
EDWARD R. MADIGAN, Illinois
MARGARET M. HECKLER, Massachusetts
JAMES M. JEFFORDS, Vermont
RICHARD KELLY, Florida
CHARLES E. GRASSLEY, Iowa
TOM HAGEDORN, Minnesota
W. HENSON MOORE, Louisiana
E. THOMAS COLEMAN, Missouri
RON MARLENEE, Montana

PROFESSIONAL STAFF

FOWLER C. WEST, *Staff Director*
ROBERT M. BOR, *Counsel*
HYDE H. MURRAY, *Counsel*
JOHN R. KRAMER, *Special Counsel*
BERNARD BRENNER, *Press Secretary*

SUBCOMMITTEE ON DAIRY AND POULTRY

CHARLES ROSE, North Carolina, *Chairman*

RICHARD NOLAN, Minnesota
ALVIN BALDUS, Wisconsin
JOHN KREBS, California
JOSEPH S. AMMERMAN, Pennsylvania
WALTER B. JONES, North Carolina
DAWSON MATHIS, Georgia
HAROLD L. VOLKMER, Missouri

JAMES M. JEFFORDS, Vermont
RICHARD KELLY, Florida
TOM HAGEDORN, Minnesota

CONTENTS

STATEMENTS

ANTIBODIES IN ANIMAL HEALTH MAINTENANCE

WEDNESDAY, SEPTEMBER 27, 1978

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

The subcommittee met, pursuant to notice, at 10:30 a.m., in room 1301, Longworth House Office Building, Hon. Charles Rose (chairman of the subcommittee) presiding.

Present: Representatives Nolan, Baldus, Krebs, Jones of North Carolina, Volkmer, Jeffords, and Hagedorn.

Also present: H. R. Gross, former Member of Congress.

Staff present: Fowler C. West, staff director; John E. Hogan, associate counsel; Glenda Temple, clerk; Carol Forbes and George Dunsmore.

Mr. ROSE. The Subcommittee on Dairy and Poultry will please come to order.

The subject of our hearing this morning is the use of antibodies in animal health maintenance for poultry and dairy cattle.

Our first witness this morning is Dr. Anson Bertrand, Director of the Science and Education Administration, U.S. Department of Agriculture.

Dr. Bertrand, will you please come forward?

You may proceed, sir.

STATEMENT OF DR. ANSON BERTRAND, DIRECTOR, SCIENCE AND EDUCATION ADMINISTRATION, U.S. DEPARTMENT OF AGRICULTURE

Dr. BERTRAND. Mr. Chairman, I am Anson Bertrand, Director of Science and Education for the Department of Agriculture.

We appreciate this opportunity to review with you the role of antibodies in animal health maintenance for dairy cattle and poultry.

Diseases and parasites of livestock and poultry are a constant threat to the profitable production of food animals. We estimate animal health problems currently cost the country about $4.6 billion per year. This is about 10 percent of the annual income derived from livestock production.

We understand the committee has special interest in protective antibodies and other biological methods as alternatives to antibiotics or chemotherapy in livestock disease prevention and control. In other statements this Department has made known its position on the use of antibiotics in livestock production to the Food and Drug Administration. Those documents are FDA dockets No. 77N–0231, 77N–0317, and 77N–0318. We believe current livestock production technology

requires varied approaches, including the use of antibiotics and other forms of chemotherapy.

Our scientists continue to give major attention in disease research to antibodies and other nonchemical methods of disease prevention and control. We have established that antibodies are substances formed by an animal in response to certain disease agents or foreign materials. Some antibodies have value in disease protection while others have value only in diagnosing disease. They are one component of a complex system that may or may not protect against animal disease. It may not be fully understood in the scientific community today.

When transferred to other animals, antibodies rapidly disappear and, unless replaced, will not provide reliable disease prevention beyond 1 to 2 weeks. Except for parental antibody transfer from milk colostrum or from the egg, the transfer of disease protection in this manner has limited use. Based on evidence to date, parental antibody is effective in preventing some diseases in young animals; however, capability for absorption from the digestive tract ceases after animals are about 24 hours old.

The duration of protection for the young depends to a great degree on the blood level of antibodies as acquired from the parent. In this type of protection, antibodies steadily decline from the blood and are usually gone by 6 weeks. They are most effective during the first 2 weeks of the animal's life.

Immunization of animals with vaccines generally overcomes the problem of rapid antibody disappearance. For many diseases, however, vaccines have not been found that will result in adequate levels of antibodies needed at the primary site of infection to prevent disease. For example, in cattle, these include diseases such as mastitis, liver abscesses, pinkeye, most respiratory diseases, and most parasitic diseases.

Protective antibodies and vaccines generally are specific for a single disease agent or a limited number of agents, and vaccines are generally ineffective for treatment once symptoms of disease are noted. On the other hand, a single antibiotic may be highly effective in preventing as well as treating a wide variety of diseases and infections.

This Department recommends several different strategies for prevention or control of livestock and poultry disease and parasites depending on the characteristics of the disease, its prevalence, and the level of technology available to deal with the problem. Continued vigilance is maintained by the Department to prevent entry of foreign animal disease into this country. Department research at the Plum Island Animal Disease Center is providing improved technology to prevent entry or assist in eradication of these diseases should they gain entry into our country. This is an area of activity that is continuing for the Department of Agriculture.

Within the United States more than 100 diseases of significant economic importance exist in our livestock and poultry. Ideally, we would prefer to completely eradicate these diseases by establishing disease-free herds and flocks. Technological and economic considerations currently make attempts at this goal impossible except for a very few problems such as brucellosis, tuberculosis, scabies, screwworms, pullorum, fowl typhoid, and chronic respiratory disease of poultry.

The Department, cooperating State agricultural experiment stations, and other cooperating institutions have substantial research in progress to develop technology needed for the control of existing diseases. Strong emphasis is being given in research to disease prevention through the induction or enhancement of livestock and poultry immunity to these problems.

The Department is currently allocating $11,895,000 to this area of research, and non-Federal funds from cooperating institutions contribute $9,824,000, making a total of $21,719,000 being spent in this area of research in the United States.

Much of this research is aimed at understanding the complex interactions and chain of events that occur when an animal or bird is exposed to a disease agent and disease or disease resistance results therefrom. Such information is required to identify and minimize toxic or other effects of disease agents. It also is crucial to identification and enhancement of disease resistance factors in the animal.

An example of this research is a Department-State cooperative study aimed at enhancing resistance to mastitis in dairy cattle. Current technology is totally inadequate to control this disease by immunization, and we must rely on preventive management and therapeutic methods.

For other diseases and parasites, we are seeking to develop new vaccines or to increase the specificity, effectiveness, and safety of those currently in use; to develop applications for resistance-enhancing factors such as interferon, immunity transfer factors, and cell mediated immunity; to improve natural resistance through improved genetics, nutrition, and management; and to develop technology for establishing and maintaining herds and flocks free of specific disease. Good progress is being made in this total effort of research; however, we must emphasize that much remains to be done and it is a long-range effort that will not reach fruition for a number of years.

In summary, Mr. Chairman, we believe the current level of livestock and poultry disease and parasite control technology requires varied strategies for best results in disease prevention. These include preventive management, the use of approved vaccines an other forms of immunization where practical and effective, and the judicious use of approved antibiotics or chemotherapeutic aids necessary to overcome current limitations of nonchemical control methods. The Department is anxious to cooperate with the land grant colleges and universities in developing nonchemical approaches to disease prevention.

That concludes my formal statement, Mr. Chairman. Thank you.

Mr. BALDUS [acting chairman]. Thank you, Dr. Bertrand, for your statement.

Chairman Rose was scheduled to make a statement before another committee. It is not unusual that we be in session and have several committee responsibilities going on at the same time.

I have some questions that were prepared by Chairman Rose. I would appreciate it if you would respond to them.

The first question is: Has the USDA ever conducted tests into the efficacy of antibodies for health maintenance of disease treatment? If so, what are the results, and who conducted them? I understand there may have been some at Beltsville.

Dr. BERTRAND. There have been some studies of this sort carried on principally in the 1960's. Studies were made of antibodies and their duration with specific regard to dairy cattle. The results of that particular study showed negative results. There was no increase in milk production or in response to the antibodies injected. This has reference specifically to a whey product that was injected.

Research of this nature is continuing in the Department of Agriculture. It is a part of many projects. I would be unable to give you additional specifics but would be delighted to provide some specifics later for the record.

Mr. BALDUS. Have you ever issued a license to anyone to market antibody treatment system? If you have, list them. If you have not, why were applicants refused?

Dr. BERTRAND. It is my understanding that a license has been issued in previous years for marketing certain products. Mr. Chairman, this was prior to my employment in the Department of Agriculture. Therefore, I would have to rely on technical help and provide the specific answer for the record later.

Mr. BALDUS. Would you provide that for the record, please?

Dr. BERTRAND. I will, yes, sir.

Mr. BALDUS. Without objection, it will be made a part of the record at that time.

[The following information was submitted:]

Veterinary biologics are regulated under the Virus-Serum-Toxin Act of 1913 (21 U.S.C. 151-158). Secretary's Memorandum No. 1744, Supplement No. 1, dated October 29, 1971, transferred the responsibility for administering the Act from the Agricultural Research Service to the Animal and Plant Health Service. Subsequently, Secretary's Memorandum No. 1762, Supplement No. 1., dated March 22, 1972, transferred the responsibility for administering the Act to the Animal and Plant Health Inspection Service.

Under the VST Act, biological products are defined in 9 CFR Part 101.2 (w) as, "all viruses, serums, toxins, and analogous products of natural or synthetic origin, such as diagnostics, antitoxins, vaccines, live microorganisms, killed microorganisms and the antigenic or immunizing components of microorganisms intended for use in the diagnosis, treatment, or prevention of diseases of animals." Analogous products referred to in this definition have included products intended for use in animals that rely upon immunological principles to be effective yet are not specifically listed in the definition.

Veterinary biological products that are presently licensed that contain antibodies and may be used in antibody treatment systems for the prevention of diseases of animals include the following:

Canine Distemper-Hepatitis-Leptospira Canicola Antiserum

Corynebacterium Pyogenes-Escherichia Coli-Pasteurella Multocida-Salmonella Typhimurium Antiserum Concentrate

Corynebacterium Pyogenes-Pasteurella Haemolytica-Multocida Antiserum

Corynebacterium Pyogenes-Pasteurella Multocida Antiserum

Duck Virus Hepatitis Yolk Antibody

Erysipelothrix Rhusiopathiae Antiserum

Escherichia Coli-Pasteurella Multocida-Salmonella Typhimurium Antiserum

Feline Panleukopenia Antiserum

Pasteurella Multocida Antiserum

Antivenin

Clostridium Perfringens Type D Antitoxin

Clostridium Perfringens Type C Antitoxin

Clostridium Perfringens Types C & D Antitoxin

Tetanus Antitoxin

This list includes only currently licensed products. Over the years, several licenses for products which have become obsolete have been submitted by licensees for termination, due to lack of interest in further production. Other licenses have been terminated to meet national eradication goals, as in the case of Hog Cholera Antiserum. These products were not included in the list, since they were not considered to be relevant to the question. The fact that many of these terminations occurred several years ago would make a complete list of such products nearly impossible to prepare.

One product that was not included on this list that was licensed under the true name of Whey Antibody Blend is considered to be relevant, however. A U.S. Veterinary Biological Product License (Special) and U.S. Veterinary Biologics Establishment License No. 258 was issued to Impro Products, Inc., Waukon, Iowa, for the production and marketing of this product on March 17, 1967. It was noted on the face of the product license that it was issued for a period of 6 months and would terminate September 17, 1967.

The firm's supporting data for this license consisted of official Dairy Herd Improvement Association (DHIA) records from Iowa dairy herds. As a requirement of the Special License, this was further supplemented after licensing with data from three other States. Many of the DHIA production records submitted by the firm were considered to be of limited value. Only data from split herds, in which part of the cows were treated with Whey Antibody Blend and the remainder were untreated controls, could be considered valid. There were seven herds consisting of 123 dairy cows, of which 55 were treated with Whey Antibody Blend and 68 were left untreated. Production records from these split herds showed an increase in milk production in treated cows compared to the controls in the same herds.

Our scientists in the Animal Husbandry Division (AHD) of the Science and Education Administration, however, pointed out that the treated and untreated cows in these experiments may not have been selected in the most objective manner. Further, these scientists indicated that other factors, such as breeding, feed, and percent days in milk, can account for increased milk production. In their analysis of the data, they were unable to determine whether the increased milk production was due to treatment with Whey Antibody Blend or other factors.

The Animal Husbandry Division agreed to conduct controlled studies to determine the significance some of these other factors may have had on the firm's results. Tests to confirm the firm's data were initiated October 3, 1966. These studies included nine dairy herds consisting of over 400 cows with approximately equal numbers of treated and control cows.

After consideration of available data, a Special License was issued on March 17, 1967, with several restrictions and requirements. One of these requirements was that results of field evaluations would be reviewed after 6 months to determine if the Special License should be reissued. It was expected that results of the AHD studies underway at Beltsville, Maryland, and additional field data from the licensee would be available for review at that time.

Results of the AHD studies that were available when the Special License terminated did not substantiate the claims made by the licensee. The similarity of the production averages between control groups and Whey Antibody Blend treated groups indicated that there were no differences that could be attributed to treatment. This was confirmed by statistical analysis. As a result, this license was not reissued.

On October 11, 1967, the firm was given the opportunity of a hearing conference with Dr. J. M. Hejl to present any additional data or arguments to support its product and the reissuing of its license. Representatives of the firm stated that the data submitted in support of the license was statistically valid and questioned the fairness of the AHD study. It was apparent that an agreement satisfactory to the firm could not be reached. As a result, it was proposed that all available data would be sent to unbiased investigators at three universities for review and evaluation. Representatives of the firm agreed to this proposal.

The firm's prelicensing data and the AHD's data were assembled and sent to Professors S. J. Roberts, Cornell University, G. E. Morse, University of Pennsylvania, and J. E. Legates, North Carolina State University. Independently, each of these scientists arrived at the same general conclusions. The firm's data lacked proper experimental design to avoid bias and possibly erroneous conclusions. Statistical analysis of these results would have little meaning and significance. Data from the AHD was properly controlled in contrast to the firm's experiments and demonstrated no significant effect on production levels or breeding efficiency. They also agreed that this license should not be reissued.

This application for license remains open, however, and numerous communications have been made with this firm concerning what additional data are needed for reissuance of the license. To date, such data have not been received.

Mr. BALDUS. Do you have jurisdiction over immunity antibody health maintenance systems of treatment or over the processes themselves? If you don't, who does? How do you classify them?

Dr. BERTRAND. Mr. Chairman, I did not understand the first part of that question.

Mr. BALDUS. Do you have jurisdiction over immunity antibody health maintenance systems of treatment or over other processes themselves?

Dr. BERTRAND. The U.S. Department of Agriculture has responsibility for research in the area of antibodies. Furthermore, the Animal and Plant Health Inspection Service has the responsibility for administering the Virus-Serum-Toxin Act of 1913. This act regulates veterinary biologics.

Mr. BALDUS. Do you consider an antibody system of treatment a biologic? What is a biologic?

Dr. BERTRAND. A biologic is a biological material that is used in the treatment of disease. The source of an antibody would be in the realm of a biologic.

Mr. BALDUS. If such a system of treatment produces scientific benefits for food-producing animals, what course of action would you take to insure that knowledge is disseminated to farmers?

Dr. BERTRAND. The Cooperative Extension Service is the arm of the Department of Agriculture that disseminates information to farmers.

Mr. BALDUS. Mr. Jeffords, do you have any questions?

Mr. JEFFORDS. You mentioned very briefly brucellosis and bringing the disease under control. I believe the way it is being brought under control is by extermination of the diseased animals. Is that generally what has happened?

Dr. BERTRAND. That is my understanding.

Mr. JEFFORDS. What research is going on in trying to find other ways to more effectively control it other than just the normal vaccination systems that have been around for years? What other kind of research is going on? How well is it funded? Where does it stand right now? How does it look for the future?

Dr. BERTRAND. Mr. Jeffords, in the 2 months that I have been employed by the Department of Agriculture I simply have not had an opportunity to get that degree of detail. With your permission, I would like an opportunity to prepare that reply and submit it for the record.

Mr. JEFFORDS. I would appreciate that very much, sir.

Mr. BALDUS. Without objection, that will be made a part of the record at that time.

[The following information was submitted:]

Following is a list of extramural and in-house bovine brucellosis research supported by SEA-AR from FY 1977 and FY 1978 funds. The list shows the nature and extent of the brucellosis research projects being funded primarily by the special FY 1978 appropriations. Those projects showing no funding for FY 1978 were funded in FY 1977 with sufficient funds to carry them through FY 1978. Research at most locations was initiated in late Spring. Most projects are designed to continue for 12 to 18 months with a few exceptions that will require several years to complete.

The research projects were designed to provide improved diagnostic tests, develop vaccines suitable for use on adult cattle, and to increase our knowledge of epizootiology and pathogenesis of the disease. The extramural brucellosis research effort has been designed to complement an expanded ongoing, in-house brucellosis research program at the National Animal Disease Center in Ames, Iowa.

Because the disease is highly communicable to cattle and man, these studies require expensive, large animal isolation facilities. Additionally, the basic research often necessitates sophisticated and expensive laboratory equipment and procedures. However, we are encouraged by the interest and participation of the various qualified scientists in universities engaged in this important research.

State institutions cooperating with the Department on brucellosis research commited a total of about $215,000 in non-Federal funds to this research in 1978. Cooperative Research, SEA, provided an additional $54,000. This research is centered on improving tests to detect brucellosis carriers, on clarification of immunity mechanisms involved in effective resistance to the disease and on the means by which the disease is spread including the role of reservoir animals in this transmission.

Research is very broad including such aspects as the role of transfer factor and phagocytes in resistance and immunity to brucellosis, the fractionation of brucella organisms to identify the role the different fractions play in the disease process, and the improvement of understanding of the disease process itself.

Current Brucellosis Projects Funded by
Science and Education Administration-Agricultural Research

Location: University of Alaska
Funds: $15,000
Title: Pathogenesis, Diagnosis, and Control of Brucella suis Type 4 Infection in Ruminants

Location: Auburn University
Funds: No FY 1978 funds
Title: Biological Control of Bovine Brucellosis by Stimulation of Cell-Mediated Immunity

Location: University of California
Funds: No FY 1978 funds
Title: Epizootiology of Brucellosis: Evolution and Taxonomy of Brucella Organisms

Location: Colorado State University
Funds: $12,500
Title: Brucellacidal Capacity of Bovine Phagocytes

Location: University of Florida
Funds: $40,000
Title: Improved Methods for Diagnosis of Bovine Brucellosis

Location: Iowa State University
Funds: $20,000
Title: Interaction of Bovine Phagocytic Cells and Brucella Organisms

Location: Louisiana State University
Funds: $40,000
Title: Immunological and Pathological Responses of the Bovine Fetus to Brucella abortus

Location: University of Minnesota
Funds: $62,000
Title: Brucellosis: Cell-Mediated Immunological Mechanisms Relating to Diagnosis and Pathogenesis in Cattle

Location: University of Missouri
Funds: $25,000
Title: Cell Mediated Immune Response by Chemical Modification of Brucella abortus Antigen

Location: Montana State University
Funds: $20,000
Title: Animal Models for Brucellosis Research

Location: University of Tennessee
Funds: $25,000
Title: Immunity to Brucellosis at Mucosal Surfaces

Location: Texas A&M University
Funds: $40,000
Title: Development of Methods for Diagnosis of Bovine Brucellosis

Location: University of Vermont
Funds: $20,000
Title: Detection of Early Brucella abortus Infection in Cattle

Location: University of Wisconsin
Funds: $80,000
Title: Cellular Interactions in Immune Response Mechanisms in Brucella Infected and Immunized Animals

Location: National Animal Disease Center, SEA-AR, Ames, Iowa
Funds: Remainder of FY 1978 brucellosis appropriation was applied in-house on the following projects:
Title: Brucella Infections in Cattle

1. Effect of reduced dosages of Brucella abortus Strain 19 vaccine in yearling heifers and heifer calves.

2. Development of specific antigens by isolation, characterization and purification of B. abortus antigenic components. Efforts concentrated on differences between Strain 19 and field strains of B. abortus.

3. Development of nonviable cell fraction vaccine capable of inducing effective immunity without adverse side effects.

4. Isolation and characterization of toxic components of virulent and attenuated B. abortus and determine effect on pathogenesis of the disease.

5. Isolation and characterization of immunoglobulins in serums from Brucella-infected animals.

6. Construction underway on four brucellosis isolation field pens.

7. FY 1978 expenses for in-house brucellosis research:

Nonexpendable equipment	$36,000
Cattle and calves	$59,000
Location support	$248,500
Personnel	$45,000
Summary - Total in-house	$583,500
Total extramural	$399,500
	$983,000

Mr. JEFFORDS. I wonder what your instructions are. We have witnesses here relative to Impro Products, Inc. I understand that you are under litigation in that area. Are you under any instructions not to answer questions relative to that?

Dr. BERTRAND. I am under no instructions, sir. I would be delighted to attempt to answer questions. However, I am not fully informed at this stage on that litigation.

Mr. BALDUS. On that point, may I ask you to stay until after those witnesses are heard in case there may be further questions of you?

Dr. BERTRAND. Yes, sir.

Mr. BALDUS. Mr. Krebs.

Mr. KREBS. Dr. Bertrand, how would you summarize, in one or two sentences, the current status of the research in the field?

Dr. BERTRAND. My summary, in brief, is that the research is continuing. It is broad spectrum research aimed at finding the most effective means of preventing disease, or of curing disease, including the use of antibodies, antibiotics, and preventive processes through management.

Mr. KREBS. As an aside, Doctor, you mentioned that it was the intention of the Department to cooperate with land-grant universities. Am I correct in assuming that the mere failure to also mention non-land-grant institutions of higher learning was nothing but an oversight on your part?

Dr. BERTRAND. That is correct, sir. You may recall that I came from a non-land-grant university to this particular position. That definitely was an oversight.

Mr. KREBS. Thank you very much.

Mr. BALDUS. Mr. Jones, do you have questions?

Mr. JONES of North Carolina. No.

Mr. BALDUS. Mr. Hagedorn.

Mr. HAGEDORN. Thank you, Mr. Chairman.

Dr. Bertrand, I understand that there are approximately 300 research projects in the field of natural immunity health systems that are either underway or about to be established. I think some are nearing completion. Are you aware of this? If so, could you bring this subcommittee up to date a little bit as to what the results might be?

Dr. BERTRAND. I believe that there are not 300 in the natural immunity health system entirely. There are approximately 300 related to animal disease research, control, and prevention.

Mr. HAGEDORN. That is right. I am sorry.

Dr. BERTRAND. A portion of them would be as specific as you indicated. Approximately 77 of those research projects are in-house projects carried on by the in-house program of the Department of Agriculture. The remaining are cooperative with the State cooperators. Those projects are all included in the broad spectrum research to which I referred a moment ago.

Mr. HAGEDORN. Do you have any feelings as to what the findings may be? Have they advanced far enough to get some preliminary information and make some preliminary judgments as to whether this is an area that has some applicability in the eradication or control of some of these diseases?

Dr. BERTRAND. May I ask for clarification? Are you referring specifically to antibody research?

Mr. HAGEDORN. Yes, I am, sir.

Dr. BERTRAND. The Department's findings to date indicate, as I indicated in my earlier statement, that the life of antibodies injected into an animal will be very short. The importance of antibodies in the young animal is extremely high. An area of research that has a tremendous potential for payoff is to find a way that an antibody may be maintained in the animal. Much of our research is aimed in that direction.

Mr. HAGEDORN. Thank you.

Mr. BALDUS. On the point of injection into the animal, has there been research done on using antibodies in feeds so that through ingestion a level of antibodies might be maintained?

Dr. BERTRAND. To my knowledge, there has not been definitive research done in this area. However, I would like the opportunity to check the record and set that straight if I am incorrect.

Mr. BALDUS. The record will be left open so that you may do that.

[The following information was submitted:]

Extensive research has been conducted on the absorption of antibody from the digestive tract of animals. Such research has shown that newborn mammals are capable of absorbing passive or short-lived antibodies for approximately 24 to 36 hours after birth from the first milk or colostrum of the dam. After that, the process of antibody absorption ceases and antibodies are degraded and digested. The level of antibody of the newborn is directly related to the level of antibody in the colostrum of the dam and the amount of colostrum ingested during the short period of absorption through the wall of the intestine of the newborn. Orally administered antibody, therefore, has little protective value in animals over 24 hours of age with the exception of certain infectious diseases of the digestive tract. Considerable research has been conducted on the use of colostral antibody for disease prevention in orphaned young, in multiple births and in other situations in which the newborn animal does not have access to the colostrum of its natural mother.

Research is being pursued on the injection directly into the host animal of vaccines to specific diseases aimed at the subsequent production of specific antibodies against the disease. Recent advances are making it possible, in some cases, to either modify or fractionate and concentrate the most immunogenic portion of the vaccines in order to achieve a higher level of protection. Thus, no research is being done on injection of antibodies into feed to be ingested because research has shown that protective antibodies administered orally are not absorbed through the intestinal wall, except for a few hours after birth.

Mr. BALDUS. Mr. Volkmer, do you have any questions?

Mr. VOLKMER. No.

Mr. BALDUS. Again, we would appreciate it, Dr. Bertrand, if you would stay in the event there are further questions. You may be excused for the present.

[The following was submitted in answer to a request from Mr. Rose:]

Question: How would USDA treat an application for interstate use of an antibody system of health treatment in conformity with USDA law? Include a discussion of how you would classify, legally or otherwise, such a process.

Answer: Assuming that the antibody system of health treatment referred to involves the use of a product containing antibodies, the Department would direct the application to Veterinary Services, Biologics Licensing and Standards staff, for consideration for licensure under the provisions of the Virus-Serum-Toxin Act of 1913. Under the VST Act, biological products are defined in 9 CFR Part 101.2(w) as "all viruses, serums, toxins, and analogous products of natural or synthetic origin, such as diagnostics, antitoxins, vaccines, live microorganisms, killed microorganisms and the antigenic or immunizing components of microorganisms intended for use in the diagnosis, treatment, or prevention of diseases of animals." A product containing antibodies intended for the treatment of diseases of animals would be considered to be a veterinary biological product by this definition, since it would be analogous to serums which also contain antibodies and are licensed for a similar purpose. Analogous products referred to in this definition have included those products intended for use in the diagnosis or treatment of animals that rely upon immunological principles to be effective but have not been specifically listed in the definition. Products that contain antibodies that are presently licensed under the VST Act include:

Canine Distemper-Hepatitis-Leptospira Canicola Antiserum

Corynebacterium Pyogenes-Escherichia Coli-Pasteurella Multocida-Salmonella Typhimurium Antiserum Concentrate

Corynebacterium Pyogenes-Pasteurella Haemolytica-Multocida Antiserum

Corynebacterium Pyogenes-Pasteurella Multocida Antiserum

Duck Virus Hepatitis Yolk Antibody

Erysipelothrix Rhusiopathiae Antiserum

Escherichia Coli-Pasteurella Multocida-Salmonella Typhimurium Antiserum

Feline Panleukopenia Antiserum

Pasteurella Multocida Antiserum

Antivenin

Clostridium Perfringens Type D Antitoxin

Clostridium Perfringens Type C Antitoxin

Clostridium Perfringens Types C & D Antitoxin

Tetanus Antitoxin

Applications received by the Biologics Licensing and Standards staff of the Animal and Plant Health Inspection Service would be reviewed for compliance with the licensing requirements for such products as indicated in the enclosed Veterinary Services Memorandum No. 800.57.

(The enclosure is held in the subcommittee file.)

Our next witness is Dr. Les Crawford, Director of the Bureau of Veterinary Medicine, Food and Drug Administration.

Dr. Crawford, would you introduce the gentleman you have with you, please?

Dr. CRAWFORD. This is Mr. Jess Stribling from my Office of General Counsel.

Mr. BALDUS. Thank you.

[The prepared statement of Dr. Crawford follows:]

Statement of Dr. Lester M. Crawford, Director, Bureau of Veterinary Medicine, Food and Drug Administration

I am pleased to be here today to discuss the role of antibodies in animal health and their status under the Federal Food, Drug, and Cosmetic Act.

BACKGROUND

Since Louis Pasteur's momentous work with biological products, scientists have been working to develop ways to immunize animals against disease-producing microorganisms and viruses.

Three groups of disease-producing agents--bacteria, viruses, and rickettsiae--include most of the infective pathogens (disease-producing agents) that plague man and animals.

The bacterial organisms, such as anthrax and tubercle bacilli, can be seen under a microscope that magnifies a few hundred diameters.

Viruses, such as of hog cholera and rabies, may be seen only with the aid of an electron microscope, which gives a magnification of many thousands of diameters.

The rickettsiae are smaller than bacteria but larger than viruses; heart-water disease (Rickettsia ruminantium) in ruminants is an example.

Nature has given animals an immunizing mechanism whereby they may acquire immunity or resistance against such infective agents. The agents stimulate body tissues to produce protective substances, called antibodies, against the disease.

When an animal becomes infected with a virus or a bacterium known to be pathogenic to this animal, it will eventually succumb or recover or it will show no visible effect of any kind.

If the animal recovers from the infection, it may have temporary or

permanent immunity to further attacks. This type of immunity is termed "acquired immunity." Animals that show no apparent reaction to inoculation are concluded to be relatively resistant or as having a degree of "natural immunity."

Both acquired and natural immunity are genetic phenomena. When an animal shows a positive reaction to a virus or bacterial attack and recovers, it means that this animal has succeeded in building up sufficient resistance by its ability to form antibodies to overcome the influence of the invasion.

The ability of the host to combat disease through the formation of antibodies has genetic implications. Without the ability to form effective antibodies, any form of vaccination or immunization of the host would be a useless procedure.

ANTIBODIES

Now what is an antibody? An antibody has been defined as "A modified type of serum globulin synthesized by lymphoid tissue in response to antigenic stimulus, each differing haptenic structure of one antigen molecule being capable of inciting a distinct response." By virtue of two specific combining sites, each of which is complementary in structure to the inciting haptenic grouping, antibody molecules combine with antigen in vivo and in vitro.

Antibodies are classified according to their behavior to electrophoresis, ultracentrifugation, and immunoelectrophoresis analyses. They are also classified according to the mode of their observed action, as agglutinins, amboceptors, antienzymes, antitoxins, bacteriolysins, blood group antibodies, cytotoxins, hemolysins, opsonins, and precipitins.

Antibodies are produced by the animal body in response to the presence of an antigen. An antigen is defined as "A high molecular weight substance or complex, usually protein or protein-polysaccharide complex

in nature, which, when foreign to the blood stream of an animal, on gaining access to the tissues of such an animal stimulates the formation of specific antibody and reacts specifically in vivo or in vitro with its homologous antibody." The antibody fraction then combats the antigenic substance and frequently completely overcomes that substance.

In order for the body to be capable of producing specific antibodies, a previous exposure to a specific antigen must have taken place. This phenomenon is termed the anamnestic reaction and is the basis of vaccination. Although it is possible in certain antigen-antibody instances for the anamnestic capability to diminish over time, there are notable examples of lifetime immunity. For instance, people exposed to swine influenza virus in 1917 were declared to be still immune in 1976.

The antigen-antibody reaction is not necessarily beneficial to the animal. Allergens are specific antigens which, upon reaction with allergen specific antibodies may release histamine which constitutes the basis of hay fever and a variety of other diseases in man and in animals.

The prophylactic use of antibodies in veterinary medicine takes several forms--including toxoids, bacterins, live bacterial suspensions, spore vaccines, live unmodified viruses, modified viruses, inactivated viruses and antisera. These are discussed in detail in the Appendix attached to my statement.

Toxoids are prepared from potent toxin which is detoxified. The active antigenic fraction precipitated with alum and, resuspended in physiological salt solution, has all the antigenic but none of the poisonous properties of the toxin.

Mr. Chairman, with that brief summary of the science of antibodies I would now like to turn to a discussion of the legal status of antibodies under the FD&C Act.

JURISDICTION

Animal biologicals are subject to both the Federal Food, Drug, and Cosmetic Act (FD&C Act), which is administered by the FDA, and the Virus, Serum, Toxin Act of 1913 (VST Act) (21 U.S.C. 151 through 158), which is administered by the Animal and Plant Health Inspection Service of the U.S. Department of Agriculture (USDA).

Section 902(c) of the FD&C Act states that "Nothing contained in this Act shall be construed as in any way affecting, modifying, repealing, or superseding . . ." the VST Act of 1913.

Manufacture

Therefore, since the VST Act provides for the licensing of animal biological products and establishments making such products, section 510.4 of the Bureau of Veterinary Medicine's (BVM) regulations (21 CFR 510.4) states that animal biologicals produced and distributed "in full conformance" with the VST Act are exempt from the premarket approval requirements for new animal drugs in the FD&C Act in 21 U.S.C. 360(b). (Furthermore, such animal biologicals are deemed to be in compliance with FDA's Good Manufacturing Practice regulations and firms licensed by USDA to make animal biologicals are not subject to the drug producer registration requirements of the FD&C Act in 21 U.S.C. 360).

If however an animal biological product is not made "in full conformance" with the VST Act and implementing USDA regulations in 9 CFR 101 through 117, it may be a new drug subject to the premarket approval requirements of the FD&C Act (21 U.S.C. 360(b)).

Distribution and Marketing

Once an animal biological product has been licensed by USDA in a USDA-licensed firm and enters into distribution channels in interstate commerce, it is subject to the adulteration and the misbranding provisions of the Act (21 U.S.C. 351 and 352). Thus, action can be taken by FDA against animal biologicals whether or not they are in full compliance with the VST for such violations as:

-- improper storage under temperatures which compromise their potency (21 U.S.C. 351(a)(2)(B)) and, if actual potency reduction is found (21 U.S.C. 351(c));
-- outdated expiration dates (21 U.S.C 351(a)(2)(B)) and, if potency was affected (21 U.S.C. 351(c)); and
-- misbranding by oral or written claims which exceed those approved by USDA (21 U.S.C. 352(a)).

If an animal biological or its producer were not licensed by USDA, then it would be subject to the FD&C Act (21 U.S.C 351(a)(5))--a new animal drug being marketed without an approved new animal drug application (NADA).

In dealing with such violative products, FDA can use its statutory enforcement authority in (21 U.S.C. 331 through 334) to seize the violative product, as well as enjoin or prosecute the manufacturer.

Residues

It is unlikely that there would be any "residues" of an animal biological. Assuming that there were, it would be within USDA's jurisdiction to establish a tolerance as part of its licensing procedure. It would also be within USDA's jurisdiction to monitor for residues in its objective monitoring program and discover any over-tolerance residues. Violative residues would be reported to the FDA for followup. FDA would attempt to determine the cause of the violation, and could take enforcement action against the violator under the FD&C Act.

CONCLUSION

Mr. Chairman, antibodies do play a significant role in preventing diseases in both animals and man. While scientists have made significant advances in protecting animals from diseases through the use of such agents, much more needs to be done before we fully understand how antibodies can further enhance our efforts to prevent diseases in animals.

Mr. Chairman, this concludes my formal statement. If you or Members of the Subcommittee have any questions, my colleagues and I will be happy to answer them.

APPENDIX

Bacterins: These are bacterial suspensions inactivated by physical and chemical means. A formalized whole culture of bacteria is called anaculture. These agents will not produce disease, but their immunizing power usually is lower than that of living agents. The maximum duration of the immunity ordinarily is not more than 12 months.

Live bacterial suspensions: These produce a more solid and lasting immunity than the bacterins. They may, however, cause the disease and should be given either in the form of attenuated strains or at an age when the effects would be the least harmful. Their effectiveness is dependent on the number of viable organisms in the suspension. Careless handling, such as failure to keep under refrigeration and permitting contamination, lowers the viable count and results in ineffective vaccination. Brucellosis vaccine Strain 19 is an example of an attenuated live bacterial suspension.

Spore vaccines: Against anthrax, suspensions of spores are used, the virulence of which has been lowered by cultivation at a higher than optimal temperature. The culture is allowed to sporulate, the cells washed from the media and the resultant suspension heated to destroy vegetative forms. Such a vaccine provides a more solid immunity than the bacterin, but is only good for one year. Because it is living, this vaccine should be used only in areas where anthrax is enzootic.

Live unmodified viruses: These confer, if properly handled, an effective and lasting immunity. They must be used with caution and given with antiserum if the virus is one which may cause an acute fatal disease like hog cholera. Otherwise, they may be given at an

age when they cause only a mild form of the disease from which animals or birds recover prior to going into production. This type of immunization is called premunizing and the result premunition. Fowl pox vaccine is an example.

Modified viruses: Such viruses are modified by serial passage through unnatural hosts. During these passages, the virus loses virulence for the natural host and becomes adapted to growth on the new host. Although losing virulence, the virus retains its antigenic properties and acts as a vaccine. These are effective and produce lasting and solid immunity. Hog-cholera-modified virus is a vaccine of this type, as are the viruses that have been adapted to grow in the embryonated egg and are used in the living state.

Inactivated viruses: These have been inactivated by chemicals, usually formalin, phenol or chloroform. Their effectiveness depends on the quantity of antigen present. Most are grown in the embryonating egg and are rich in antigen. The immunity produced is strong in most instances, but vaccination should be repeated annually. In some cases, two injections are recommended.

Antisera: These are hyperimmune sera originating from a variety of sources depending on the specific antigen. Some are homologous because the antigen is active in only one species. When other than homologous serum is used, anaphylactic reactions may occur. Included in this group are the antitoxins. Immunity is present immediately following the administration of an antiserum, but is of brief duration. Antisera are used prophylactically and therapeutically in certain viral bacterial diseases.

Mr. BALDUS. I have some questions that have been prepared by the chairman.

Has FDA ever conducted tests into the classification or efficacy of antibodies for health maintenance or disease treatment? If so, what were their results and who conducted them?

Dr. CRAWFORD. The Food and Drug Administration, to my knowledge, limits both intramural and extramural research to those areas over which we have jurisdiction. We do not have, and have not since our inception, jurisdiction over the approval of animal biologicals. Therefore, such research as may have been done within the Federal research establishment would in all likelihood have been funded by U.S. Department of Agriculture. To my knowledge, we have not conducted research in the use of antibody health maintenance.

Mr. BALDUS. Neither the Department of Agriculture nor you folks claim jurisdiction. Have you ever discussed that between you?

Dr. CRAWFORD. Yes. We have had discussions relative to when a product is a drug and when it is a biological. When it is a drug and is intended for animals, then it is our jurisdiction. When it is a biological, or a vaccine of some sort, it is the jurisdiction of USDA. However, in some circumstances, once a compound has been cleared for introduction to the marketplace, and it is an animal biological, then it is provided in our act that we may seize the product if it is mislabeled, misbranded, or if it is suspected of being adulterated or incompetent to do what it is supposed to do, that is, to convey immunity. However, until the product gets on the market, it is not within our bailiwick.

Mr. BALDUS. How do you define the jurisdiction of the USDA then?

Dr. CRAWFORD. The jurisdiction of the USDA, as I understand it, under the Virus, Serum, and Toxin Act, has to do with this. They accept data from firms that wish to introduce animal biologicals and judge them on their merit. Then they make a judgment as to whether or not they should be approved for use in the United States.

Mr. BALDUS. Then would they license?

Dr. CRAWFORD. They would be empowered to license. We are not empowered to do that.

Mr. BALDUS. How would you classify such a treatment system based on the antibody concept—food additive or new drug—requiring extensive application procedures or what? What about a biologic or blood serum? Why?

Dr. CRAWFORD. If we judge—and we do get these from time to time—that an application is a biological rather than a drug, then we forward that to the USDA with a cover letter.

Mr. BALDUS. In other words, you would make that judgment and then simply give them the jurisdiction.

Dr. CRAWFORD. Yes, However, there are gray areas where we have some difficulty determining what the product is intended to be, but these would be rare.

Mr. BALDUS. In order to define that, because in the question here is the term new drug, you would have to decide whether or not it was a drug or an antibody?

Dr. CRAWFORD. Yes.

Mr. BALDUS. The extensive application procedures would follow the first determination as to whether it was a drug or an antibody?

Dr. CRAWFORD. Yes.

Mr. BALDUS. The question refers to blood serum.

Dr. CRAWFORD. Hyperimmune blood sera actually contain antibodies. The term blood sera simply means a defined portion of the blood which is called serum is extracted, harvested, and marketed, for the purpose of conveying antibodies to the animals. This would make it an animal biologic.

Mr. BALDUS. What resources would be necessary to make a determination as to the efficacy of such a system of treatment through the use of an antibody serum?

Dr. CRAWFORD. This is not within our purview. We do not have established guidelines for that, USDA does.

Mr. BALDUS. You would yield to USDA on that question?

Dr. CRAWFORD. Yes.

Mr. BALDUS. Mr. Jeffords.

Mr. JEFFORDS. As you know, we are having a witness today relative to a product put out by Impro Products, Inc. Can you tell us what involvement you have had with that particular product, if any?

Dr. CRAWFORD. I have had no personal involvement. However, our records show that we made a determination in concert with USDA that certain products manufactured by that corporation were within their purview and others were within the purview of FDA. As I understand it, some products manufactured by Impro are animal drugs; others are animal biologicals. We simply made a distinction together with USDA.

Mr. JEFFORDS. Which ones are you involved with in FDA?

Dr. CRAWFORD. We are involved with a product called Teat-Tone, and I believe there is one other, Mr. Jeffords. I will have to check that and enter that into the record.

Mr. BALDUS. Without objection, the record will be held to receive that.

[The following information was submitted:]

The second product that FDA is involved with is Teat-Treat.

Mr. JEFFORDS. Also, along with that would you get us any reports or any actions that you took relative to that product?

Dr. CRAWFORD. Relative to the product over which we have jurisdiction?

Mr. JEFFORDS. Yes.

Mr. BALDUS. Without objection, the record will also be held to receive that.

[The following information was submitted:]

On November 28, 1977, quantities of Teat-Tone and Teat-Treat were seized as being adulterated in that they are new animal drugs which are unsafe since FDA has not approved them for marketing. Default was entered against the products on May 4, 1978 (documents attached—Seizure).

[The documents attached are held in the subcommittee file.]

Dr. CRAWFORD. We have had two seizures on that product because we do not believe it is in conformity with the Federal Food, Drug, and Cosmetic Act.

Mr. JEFFORDS. For what reasons did you believe it was not in conformity?

Dr. CRAWFORD. The firm manufacturing the product has not submitted data that we have approved that establish it as a marketable drug.

Mr. BALDUS. Mr. Krebs?

Mr. KREBS. Doctor, when you stated a minute ago that you had two seizures, what did you mean by that? Would you elaborate on that?

Dr. CRAWFORD. Yes. We confiscated drugs that were marketed in interstate commerce not in compliance with the Federal Food, Drug, and Cosmetic Act.

Mr. KREBS. On what fact or facts did you base your conclusion that they did not conform with that act?

Dr. CRAWFORD. They are not approved by the FDA for marketing.

Mr. KREBS. That is a violation of Federal law; is that correct?

Dr. CRAWFORD. Yes.

Mr. KREBS. Have they ever been submitted to you for approval or disapproval?

Dr. CRAWFORD. Some information has been submitted. That information that has been submitted has not been adjudged to indicate that this product should be marketed.

Mr. KREBS. Presumably this was conveyed to the producers of this particular product; is that correct?

Dr. CRAWFORD. Yes.

Mr. KREBS. How long ago was that, roughly?

Dr. CRAWFORD. This goes back several years. I think 4 or 5 years.

Mr. KREBS. Since this rejection, for lack of a better description, by your Department of this particular product, has this product been resubmitted?

Dr. CRAWFORD. There has been continuing information relative to it. There has been communication with the firm as late as this summer relative to some continuing concerns, as I understand it, by the firm to market the product. We are continuing to work with them.

As you know, our position is that, if they can submit data which shows that the compound is both safe and effective, then we will expeditiously allow the marketing of it. However, that judgment is empowered to us by law.

Mr. KREBS. I am not that familiar with the procedure that is involved. Have they in essence resubmitted their product for further evaluation by your department?

Dr. CRAWFORD. I will have to check the record, I do not think it has been a formal resubmission. I would have to characterize it as continuing dialog. However, I will check the the record and bring it up to date.

Mr. KREBS. Thank you very much, Doctor.

Mr. BALDUS. Without objection, the record will be held at this point for that purpose.

[The following material was submitted:]

Following the seizure action, Impro submitted revised labeling for Teat-Sof (Teat-Tone) and Teat-Neat (Teat-Treat) to remove drug claims and label the products as cosmetics. The products continued to be recommended for use on the teats of dairy cattle which could result in milk residues. As such, FDA concluded that Impro would be required to submit a food additive petition to provide for the use of these products in dairy cattle (documents attached—Food Additive).

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
ROCKVILLE, MARYLAND 20857

COPY

June 14, 1978

Robert A. Collins
Impro Products, Inc.
Waukon, Iowa 52172

Dear Mr. Collins:

This is in response to your letter of January 6, 1978 concerning Impro "Teat-Sof and Impro "Teat-Neat."

These products with the revised labels do not constitute animal drugs. This conclusion is not based on the presence of the statement "Cosmetic" nor the disclaimer concerning its use as a sanitizer, but on the change in names and the deletion of the therapeutic claims. If the products were approved food additives, this labeling might be suitable for use (with the deletion of the disclaimer on Teat-Neat), however, it would be premature to approve labels on an unapproved product.

Your products as presently formulated for their intended use are unapproved food additives. We base this conclusion on possible milk residues related to the use of these products. You have previously been made aware of our concerns with pine oil and castor oil. We are enclosing a copy of 21 CFR 571, which outlines the procedure to follow in submitting a food additive petition.

In an attempt to respond to your questions concerning pine oil methodology, we had our chemists contact several individuals. We wish we could be of more assistance, however, because of the variablility in pine oils and because we do not know the specific composition of yours, we are not able to suggest a method. There is no official method. The ultimate responsibility for developing a suitable method lies with you. We will be glad to assist you in the future if we can.

Sincerely yours,

Judith Gushee
Consumer Safety Officer
Case Guidance Branch
Bureau of Veterinary Medicine

Enclosure
As Stated

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
ROCKVILLE, MARYLAND 20857

Honorable Michael T. Blouin
House of Representatives
Washington, D.C. 20515

JUN 19 1978

Dear Mr. Blouin:

This is in further response to your letter of May 16, 1978, to Dr. Van Houweling, concerning Impro Products, Waukon, Iowa.

Specifically in your letter, you questioned two inspections made since revised labels were submitted to the Division of Compliance, Bureau of Veterinary Medicine, Food and Drug Administration (FDA). The inspection of March 14, 1978 was a general inspection. FDA had not performed a complete inspection of this firm since January 20, 1977. It is a statutory obligation that drug firms required to register be inspected at least once every two years. For a firm which is not in compliance, increased surveillance is not uncommon. An investigator was also at this firm on April 25, 1978 to gather information concerning their recall of promotional material. It is standard operating procedure to gather information from a recalling firm before and after the recall. At the initiation of the recall, information including the name of the product involved, the consignees, the reason for the recall and the procedure the firm intends to follow is obtained. At the conclusion of the recall, a summary of the recall effectiveness is prepared. This information includes the amount of product recevered and disposition of the product. Impro Products has not been subject to any further inspectional activity than any other firm subject to a recall, a regulatory letter and a seizure. When it becomes necessary to visit a firm, we limit our visits to only the collection of information necessary. The statutory obligation inspection is the only type of inspection in which all facets of the firm's activities are reviewed.

We do not believe, as stated in your letter that we instructed the firm to market their products as cosmetics instead of drugs. The firm was told that the deletion of the therapeutic claims may cause the product to constitute a cosmetic. Neither the FDA nor any other agency, of which we are aware, has any jurisdiction over animal cosmetics.

In response to our actions, the firm submitted revised labels without therapeutic claims labeled prominently "cosmetic." Because of this, we reevaluated the safety of the product and we carefully considered the apparent disclaimer. We have concluded these products constitute food additives and to continue marketing these articles the firm will be required to submit food additive petitions pursuant to 21 U.S.C. 348 and Title 21, Code of Federal Regulations (CFR), Part 571 and have them approved. The products are obviously intended for use on teats of dairy cattle so it may become incorporated into the milk. Thus, safety of such use must be shown. Impro Products is being advised of this by separate letter.

We wish to assure you that the Agency has no desire to harass this firm and that our activities have been wholly consistant with the spirit and the letter of the law. Please let us know if we can be of any further assistance.

Sincerely yours,

Robert C. Wetherell, Jr., Director
Office of Legislative Services

Mr. BALDUS. Did you make the decision that that was within your jurisdiction at sometime during that period?

Dr. CRAWFORD. Yes.

Mr. BALDUS. Mr. Hagedorn.

Mr. HAGEDORN. I have no questions.

Mr. BALDUS. Mr. Volkmer, do you have questions?

Mr. VOLKMER. No.

Mr. BALDUS. Dr. Crawford and Mr. Stribling, we would ask you to stay through the testimony of the next witness because that might be helpful.

The next witness is Ms. Mary Collins, secretary/treasurer of Impro Products, Inc., Waukon, Iowa. She is accompanied by Dr. Richard Campbell, veterinarian, Lewiston, Minn., and Mr. Bill Schmidt, dairy farmer, Sturgeon Bay, Wis.

For the record, I think I should note that Ms. Collins resides in my district in Wisconsin. However, I want to make clear for the record that the hearings today are because of the interest and concern of the chairman, Mr. Rose, not of any special consideration from myself.

Ms. Collins, you may proceed.

STATEMENT OF MARY COLLINS, SECRETARY/TREASURER, IMPRO PRODUCTS, INC., ACCOMPANIED BY DR. RICHARD CAMPBELL, VETERINARIAN, LEWISTON, MINN.; BILL SCHMIDT, DAIRY FARMER, STURGEON BAY, WIS.; AND GEORGE QUALLEY, LEGAL COUNSEL TO MS. COLLINS

Ms. COLLINS. My name is Mary Collins. I am from Waukon, Iowa. My sister lives in Wisconsin, Mr. Baldus, and I met you at a meeting with her.

I would like to express my sincere appreciation to the chairman and members of this subcommittee for the opportunity to tell the story about the work that we have done on a tremendously fine product.

For the last 15 or 20 years we have been privileged to work with a very simple product. We produce an antibody in the udder of a dairy cow. To accomplish this we take a chilled vaccine of whatever bacteria we want to work with. We infuse it in the udder of a cow every week for at least 3 weeks before that cow calves. When that cow calves, in order to protect her young in her milk she has antibodies or immunocompetent factors, which we then harvest from the milk and use as products to inject in animals and use orally on both animals and man.

This product has no parallel in safety in the history of medicine. We have gone so far as to replace one-half of the blood of a dog with this product with no side reactions.

During the years we have had an opportunity to work with many great people: Dr. Reyneir at Notre Dame, who developed germ-free life, and Dr. Young from the University of Nebraska, who developed specific pathogen-free pigs. We have worked with many fine physicians and veterinarians.

I want to take just a few minutes to review some of the work that we have done in the human field because this question of whether

you can absorb an antibody that is produced in the udder of a cow has just got to be different than antibodies produced in blood.

Ten or fifteen years back we were working with staph 80 and 81, which is the hospital staph that was causing so many problems with a very high rate of death. Our family physician caught us one day and had a 50-year-old patient with staph pneumonia. She was diabetic. They had run sensitive drugs on the bacteria. It showed resistance to all the antibiotics except two. When they used the two drugs, it kicked the diabetes completely out of control so they had to quit.

She took the staph 80 and 81 product orally because she was in a semicomatose state at this time. Within 48 hours they saw some visible improvement in the patient. Within 72 hours they could not culture the staph. The pneumonia was cleared up.

Shortly after this there was a little 4-year-old girl in our town who was severely burned. Over 60 percent of her body was burned and 37 percent was third degree burns.

It is fantastic what they can do on burn patients as far as shock and getting the kidneys operational, but the infections are a terrible problem in burn patients. First Peggy came down with a staph infection. She was in the hospital in Minnesota. They finally got that under control with medication. Then she developed a pseudomonas septicima infection and it went into complete blood poisoning.

At the time we had prepared a pseudomonas product to do some testing in urinary tract infections. Because I knew the people and I knew this little girl, I called one of the physicians with whom we were working and asked, "Is there any possibility that this product can be used on Peggy because the doctors have told her parents that she can't live?" He said, "If it is pseudomonas septicima, nobody has lived with it but I don't think we have any other choice but to at least make this product available."

She had run a temperature at this time of up to 105 every day for 21 days. It would peak and they would get it down. She was critically ill and on I.V. They did not know how much of this she could absorb orally and they tubed it.

Within the first 24 hours she absorbed almost an entire quart of this product. At 48 hours they decided she seemed somewhat better. At 72 hours the pseudomonas had disappeared out of the blood. It was a long, several month period before they could no longer culture the pseudomonas from the open area of the burn. But when they do the graft it is real touchy following pseudomonas because the toxins tend to come out through the skin. When they do the graft it is critical because, if 50 percent of that graft does not take, then the open area is overwhelming. When they did the graft on Peggy, 90 to 95 percent of that first graft took.

The physicians reported to us that she was the first person in the history of medicine who ever lived with pseudomonas in the blood.

When she came home she was 4 years old. I have some pictures of her I would like to pass out. They had drawn her arm to her to cover area and she had been a very sick little girl. She is now 19 years old and a college sophomore. She does competitive swimming and plays golf. So it is very difficult for me to believe that you cannot absorb the antibody or protective factor that we produce in the udder of a dairy cow through the GI tract.

35-830 O - 79 - 3

I think this is what very probably has presented many of the problems. Stop and think. Neither of these products that we used on these two human patients can be measured by any scientific test now known. The other thing is the fact that the product was absorbed through the GI tract because this is how it was administered. Both of these facts would take us right out of being a biologic.

I want to take a little bit of time to consider two other great things. In my own mind I relate our product to them.

One is the gift of electricity that we get from nature. No one knows what electricity is except by what electricity does. Six hunderd years before the time of Christ, they had observed the phenomenon of electrical attraction. Of course, in 1800 with Edison the great work was done.

If these people had not been able to work with and use electricity before it could be identified—and it cannot be identified today with the electron microscope—we would be stumbling around in a pretty dark world.

With vitamin C, too, way back in the 1500's when 100 out of 160 sailors would die from scurvy, the British found out that if they gave them lime juice and gave it to them everyday then the death loss dropped. People have observed and used vitamin C for the 200 years up until 1927 when vitamin C was actually identified and classified.

For 10 years we have been working with dairymen in the Midwest producing our product on an intrastate basis after our license was canceled by the Division of Biologics. We have been working with top-flight dairymen. Bill Schmidt is one of them from Wisconsin. He milks 100 dairy cows. He knows what it is to produce milk. He knows what it is to produce milk without using antibiotics routinely.

We have worked with people like Dr. Campbell, a veterinarian from Minnesota who has worked and observed our product through the 10 years.

I asked these people to come with us today to give you an opportunity to ask questions of them.

I want to take a little time to review our licensing. We submitted field data to the Division of Biologics back in 1965 showing an increase in milk production of about 1,500 pounds on the average with the dairymen who were using these antibody products. They gave us a 2-year license to continue this testing all over the United States and acquire much field data, which would have been perfect.

However, we ran into a stumbling block. In 1963, a Dr. John Herrick, an extension veterinarian from Iowa State University, came to us and asked us for $100 a month in order to promote our product and help with clearances. I think what we ran into is the story of what happens when you don't pay this.

Before they had time to issue our license that they promised us, USDA from Beltsville called and demanded to run a test on this product. We had to furnish the material. This test was run by five scientists in the USDA. Within 6 months they submitted reports that this product was worthless. Our license was canceled.

This negative data was rushed to be published in outstanding scientific publications, such as the Journal of Dairy Science and the American Veterinarian Medical Journal. When data is published there, it misleads many innocent people. Once it is published in a

prestigious scientific journal, the total effect, even if truth is known, is never erased from the minds of many scientists.

At this time I went to Congressman H. R. Gross. I said, "Mr. Gross, if we cannot get the actual data on this test, we are totally out of business." Through his effort we were able to get this data.

The truth of what this test showed is that out of 460 animals in that test 60 Impro cows were injected according to the test plan and 48 control cows were injected according to the test plan. Nine cows were injected 19 days before the product was made available. Five cows were injected 18 days before the product was made available.

As phony as this test was, if you take the cows that were injected according to the test plan, the Impro cows showed a 1,021 pound milk increase advantage.

I am asking this subcommittee to investigate this test that was used to cancel our license and that is being used today to malign our work. Let's get the truth of this test out on the table and then take our research and product from there.

If you have questions on production or other work, we will be glad to respond.

Thank you very much.

[The prepared statement of Ms. Collins appears on p. 73.]

Mr. ROSE. Thank you very much.

Are there questions from members of the subcommittee? Mr. Jeffords.

Mr. JEFFORDS. What kind of system have you used to follow the animals that have been treated with your product to determine the long-term effect of it?

Ms. COLLINS. This was one reason why we concentrated so heavily in the dairy area. There are official dairy herd improvement records. This is where a Government employee goes to the farm each month and weighs the milk from the cow and figures the fat. Therefore, all the production records showing this increase in production are done not by the farmer and not by anyone from our company but by a third person. The other good part about this is that the breeding records are available. So you can see if you have had improvement in conception. What happens to the cows is available.

All of the records that I submitted to the committee on the 5,200 lactations have official DHIA records where you can go back and check on any individual cow.

Mr. JEFFORDS. Is there an analysis done comparing those which utilize the product with those from the same breeding lines that were not treated with it to determine the difference in the milk production?

Ms. COLLINS. Yes. As a matter of fact, I would say the best work that was done with that was done at Beltsville, Md.

According to their test play, all their heifers would have to be from split sires. In other words, if a sire had two daughters in the herd, one would be a test animal and one would be a control animal, which is the only thing you can do with heifers because they do not have previous records.

In the Beltsville test itself there are a few cows that were injected off timing, but they had 16 cows in the Impro group and 14 cows in the control group that were half-sisters. They were all heifers, so you would remove part of the genetic variation and the age factor.

In this test the Impro cows produced 2,231 pounds of milk more than the control cows. They also produced considerably over the bull provings on their record.

Does this answer your question?

Mr. JEFFORDS. All the other factors, such as feed, were——

Ms. COLLINS. They were all exactly the same, yes, in the Beltsville herd.

Mr. JEFFORDS. Over what length or period of time did that take place?

Ms. COLLINS. That took place during the first calf lactation. Mr. Schmidt would have records available for you from over a 4-year period. He is using the product on all his cows.

Mr. JEFFORDS. Is this product a thyroprotein? Is that how you describe it?

Ms. COLLINS. No. This product is a natural antibody, although it is not measurable with any test they have now. There is much not known about antibodies and the ability to measure them.

No, this is a natural antibody produced in the udder of a cow. It is part of the milk that we take from that cow after she drops her calf. It is just an antibody. The immunocompetent factor that is there is put there by nature to protect the calf. We then extract it and use if on animals and people. We predetermine what we are working with by the antigen we use.

Mr. ROSE. Would the gentleman yield?

Mr. JEFFORDS. Yes.

Mr. ROSE. I want to thank you for your testimony, I want us to continue it, but I would like to say something at this point in the record.

The reason that I asked you to come here and the reason that we want to hear from you and your veterinarian and people who have had experience with antibodies as produced by you and your organization is that we are constantly told by the bureaucracy that antibiotics in certain situations can be very harmful and that they are considering banning them, restricting their use, and requiring veterinarians to be present for their administration.

I do not have an opinion about that particular subject, nor do I have a firm opinion about your particular approach to the health of dairy herds. However, I do notice what I consider to be almost a criminal negligence on the part of the bureaucracy that on the one hand is telling us current methods are unacceptable, yet exhibiting a total unwillingness to give every possible evaluation to methods such as those that you have brought forth.

I hope that the USDA and the FDA will hear us very clearly when we tell them, "Don't come up here telling us antibiotics don't work or are improper for certain situations on the one hand and then show the kind of benign negligence that these test results show," which H. R. Gross got and gave to you from the Beltsville experiment. The two positions are just not acceptable.

You have given us a list of cows that have been treated in the so-called Beltsville test. It says "to Senator Gross."

I guess Senator Gross did act like a Senator when he was here. That says something about Agriculture's perception, which might fall over into the results, you know, if they could not tell a Senator from a Congressman.

Did you not give us some results that H. R. Gross gave you, which you were told came from Beltsville? Is that correct?

Ms. COLLINS. Yes.

Mr. ROSE. You have a column here called "Date Injected." There is a copy of this in every member's folder who is on this subcommittee. We have circled almost all those cows. Aster, Belinda, Beryl, Cherry, Christie, Connie are some of the cows' names. They have been injected and you have indicated that they are not eligible. Would you explain what that means?

Ms. COLLINS. Yes, I will.

When Beltsville set up this test, they submitted a protocol or plan of the test, which naturally included following the directions for the use of our product. In this cows were to be injected 5 to 7 days previous to calving with 50 cc's of Impro. When I finally got this test, through the help of Representative H. R. Gross, we found out that these cows had been injected anywhere from 42 days previous to calving up to 5 days following calving. There isn't a dairyman I have ever worked with in my life who would not know when a cow had calved.

We took this test, Mr. Rose, and we went to 10 days, to give them extra leeway. We circled in blue the cows that were injected according to the protocol of the test. These are the animals I referred to when I said they showed an increase of 1,021 pounds of milk over the control cows.

The pitiful part about this test, when you look at this, is that it does not tell who they were injected by. Some of the dates they were injected are not listed. Some say "probably injected."

This was the type of work that was used to take our license.

Mr. ROSE. Thank you, Ms. Collins.

I have just been informed that our great friend and former colleague, Congressman H. R. Gross, is in the audience.

Congressman, would you let us recognize you? We appreciate your being here today. Thank you, sir.

I would say to our friend that the place has not been the same since you left. Mr. Bauman tries to carry on in the best tradition but he doesn't match your style, sir.

Mr. JONES of North Carolina. If it is in order, I would like to invite Mr. Gross to sit with us.

Mr. ROSE. Is there any objection?

[No response.]

If not, we welcome you to come and sit with us if you so desire, Mr. Gross.

Mr. Krebs, I believe you have questions.

Mr. KREBS. Yes.

Ms. Collins, I am going to ask you a question and I don't want you to read any negative connotations into it.

Ms. COLLINS. I won't.

Mr. KREBS. Apparently somewhere along the line I missed your educational and professional qualifications. Would you be kind enough to give me some idea as to that?

Ms. COLLINS. I would be happy to do so.

Mr. KREBS. Thank you very much.

Ms. COLLINS. When I finished high school, it was during the war. I had a younger brother and sister, and we had three farms. I went into the real estate business right away and managed the farms. I went to college very shortly on a part-time basis. I have had the opportunity, since I got into the field on antibodies, to have worked with some of the very top scientific people in the United States.

My brother who works with me is an engineer. I think that is an excellent background because engineers have a certain logic.

I do not have a scientific background. I am a farmer, a businesswoman, and I know a lot about antibodies.

Mr. KREBS. As I gather from your testimony, you are the one who, with the help of some of your relatives, conducted these various tests; is that correct?

Ms. COLLINS. No. This test to which I am referring was conducted at Beltsville. The field data to which I am referring that we use and which was submitted to you is all done by DHIA herdsmen. They are complete herds. I do not want you to misunderstand me.

It is just like with Peggy. There was not any split there. They did not have another little 4-year-old girl that they let die. However, they assumed that because they gave her these antibodies against pseudomonas—and she is the first person in the history of medicine who lived—that it is highly likely that the protection was produced in the udder of a cow and ingested through the GI tract.

We are doing much work in the human field. I did not want to take up the time on this now, but this is where our splits are coming.

Mr. KREBS. Thank you very much.

Mr. BALDUS. Congressman Nolan?

Mr. NOLAN. Did I understand you to say that in your judgment some of the dates in here were either inaccurate or deliberately falsified?

Ms. COLLINS. I am not saying that they are inaccurate or falsified. I am saying this is the way the work was done, Representative Nolan. There were 14 cows injected 3 weeks before we even delivered the product.

Mr. NOLAN. I wanted to make sure I understood that correctly. So there either was an error or it was deliberately falsified in this report.

Ms. COLLINS. You will have to make that decision.

Mr. NOLAN. Mr. Chairman, have we had, or do we intend to have, someone from Beltsville come in and give us testimony?

Mr. ROSE. If the gentleman would yield at that point, I would like to ask Dr. Bertrand to please answer some questions.

Are you familiar with these tests?

Dr. BERTRAND. Mr. Chairman, I am aware that the tests were run. I have been briefed by the scientists that conducted them very briefly. I would be unable to answer specific questions, but I would be delighted to provide for the record whatever the subcommittee would like.

Mr. VOLKMER. Are the scientists who conducted the test still at Beltsville?

Dr. BERTRAND. At least one of them is, sir.

Mr. VOLKMER. Where is the other one?

Dr. BERTRAND. I do not know. They may also be at Beltsville. I have only contacted one of them.

Mr. VOLKMER. I suggest that we bring those gentlemen in.

Mr. ROSE. I think that is certainly in order.

Dr. Bertrand, what sort of information did they give you about these tests?

Dr. BERTRAND. They outlined the procedure that you have heard discussed this morning. To my knowledge, the report that has been given relative to the nature of the conduct of the test using cooperating herds is correct. I know the record that has been submitted is the record of the scientists' data; that is an authentic record. You have here in the testimony this morning the record of the experiment.

Mr. NOLAN. At a minimum, it would be helpful to us, Dr. Bertrand, if you could prepare a statement for the committee in consultation with the scientists who participated in this experiment, documenting how as a practical matter injections were in fact made considering the fact that the suppliers have given testimony that there was none available at the time.

I would like to ask the chairman to consider inviting the scientists to come and give testimony.

That is the only question I have right now.

Mr. ROSE. Dr. Bertrand, I would like to emphasize what Congressman Nolan has said and also ask you to please submit for the record the names, titles, and current locations of the scientists in Beltsville who conducted this test, if you can.

[The following information was submitted:]

Explanation of how injections were made in cows when no antibody product was available to the farmers.

During the September 27th hearing, Miss Mary Collins showed the Subcommittee members a work sheet (enclosed) which showed that one of the farmers cooperating in the experiment had injected his dairy cows with a solution on September 4th and 5th, 1966, prior to the date on which the farmer received a supply of IMPRO Whey Antibody Blend which was to be used in the experiment. This data was supplied to Congressman H. R. Cross in response to a letter he wrote to USDA on August 6, 1969. Scientists answering his letter were instructed to transcribe all information as it appeared in their files.

We believe that the farmer made an error in recording the dates of those injections, which probably were administered on October 4th and 5th rather than September 4th and 5th. Our explanation follows:

On Tuesday, August 30, 1966, Miss Mary Collins, representing IMPRO Products, Inc., and Dr. Davidson, representing the Veterinary Biologics Division of the Agricultural Research Service (ARS), met with scientists in the Dairy Cattle Research Branch of ARS to discuss information presented by the company to the Department regarding IMPRO Whey Antibody Blend. The group discussed the possibility of the U.S. Department of Agriculture's participating in some planned controlled testing on the efficacy of IMPRO Whey Antibody Blend in increasing the milk yield of dairy cows.

The Director of the Dairy Cattle Research Branch decided that scientists in his unit should undertake such controlled testing of the product. The Beltsville scientists selected the Beltsville dairy herd and eight herds of milk cows on farms located throughout the State of Maryland to be used in the tests. General arrangements for the USDA testing are contained in a memo written Friday, September 2, 1966, by Dr. R. D. Plowman, Leader, Genetics and Management Investigation, Dairy Cattle Research Branch, ARS, to Dr. G. V. Peacock of the Veterinary Biologics Division of ARS.

It is our understanding, based on the recollection of Dr. James Smith, one of the scientists involved in the 1966 experiment, now a research animal scientist at the Beltsville laboratory, that each of the eight farmers whose herds participated in the experiment was visited a few days before he began the experiment on his farm. During the visit, the scientists selected the cows to be tested from Dairy Herd Improvement data, provided the IMPRO Whey Antibody Blend, the control solution injection, instructions on how to inject the cows, and blank forms on which to record the date of injection and the product injected in each cow. The first

farmer to initiate the experiment did so on October 3, 1966. Evidence that he began the experiment on that date is contained in a November 1, 1967, letter from Dr. J. M. Hejl, Director, Veterinary Biologics Division, ARS, to Congressman H. R. Gross. The relevant portion of the letter (which is enclosed) follows:

> What date was the test started?
>
> > The first cooperating dairy herd was started on October 3, 1966. The other herds were started during the succeeding two weeks.

Finally we would like to point out that September 4, 1966, was a Sunday and that September 5th was Labor Day. To the best of Dr. Smith's recollection, the Beltsville scientists would not have had time on Friday, September 2nd, the date of the memo mentioned above, to visit any one of the farmers to secure his cooperation and to select experimental cows, prepare the control solution injection, supply hypodermic needles, and give him blank forms on which to record his experiment data. Thus it does not seem possible that one of the farmers could have begun injecting his cows on Sunday, September 4th.

Dr. Smith says that no farms were visited until the Beltsville scientists received the IMPRO Whey Antibody Blend. He does not recall when the IMPRO shipment was received in Beltsville, but Miss Collins' testimony before the Subcommittee said she took the IMPRO to be used in the test to Washington on September 23rd.

Cow	Group	Date injected	Date calved	Remarks: (Record any observed condition as udder edema, mastitis, calving diff and general health)
G02	1	9-4-66	9-4-66	Didn't Clean
I66	3	9-4-66	(9-4-66)	—
D13	1	9-4-66	10-9-66	
G13	3	9-4-66	10-8-66	
E57	1	9-4-66	10-13-66	
G64	1	9-4-66	10-12-66	
G78	1	9-4-66	10-15-66	Pulled Calf
G66	3	9-4-66	10-16-66	
I79	3	9-4-66	10-13-66	
I68	1	9-5-66	10-19-66	
I71	1	9-5-66	10-13-66	
I90	3	9-5-66	10-13-66	Normal Size Calf- Born Dead
I82	3	9-5-66	10-19-66	
E61	1	10-10-66	10-9-66	Made Error
I40	3	10-10-66	10-17-66	
I49	1	10-13-66	10-14-66	Pulled Calf
I51	3	10-10-66	10-17-66	Pulled Calf
I[illegible]	1	10-10-66	10-19-66	Pulled Calf
H87	1	10-12-66	10-11-66	
~~X093~~	~~1~~	~~10-15-66~~		~~Bottom Broke Down~~
I65	1	10-13-66	10-15-66	Pulled Calf
F16	3	10-17-66	10-20-66	
I85	1	10-20-66	11-2-66	
I91	1	10-20-66	11-2-66	
H73	1	10-20-66	11-6-66	

September 2, 1966

To: G. V. Peacock

From: R. D. Plowman

Subject: Evaluation of Impro

I am enclosing two documents for your consideration. The first concerns an evaluation of the data supplied by Miss Mary Collins in support of Impro as an aid in increasing milk production. It is my professional opinion that she has shown no conclusive proof that Impro caused the observed changes in milk yield. Other things could have been responsible. There is enough suggestion of a benefit to be derived from this product, however, that we would like to experiment with it, to assess its true value.

The second document is a brief project outline which describes our proposed experimental procedure. If you concur in this, please make arrangements for delivery of Impro to us so that we can get started on the project at an early date.

ARS:AH:RDPlowmanPapn 9-2-66

Evaluation of Data Concerning Impro

1. Complete herds treated.

It is very difficult to evaluate the causes of production changes in a herd from one year to another. Such things as quality and amount of feed, disease, and disorders, amount of culling, age of herd, reproductive efficiency, labor supply, etc., all have large effects on total herd production. Unless all of these sources of variation are taken into consideration and evaluated, it is almost impossible to determine the specific effects of Impro.

Example - Andrew Schulte Herd

	Feb. 1962	1963	1964
% days in milk	80	85	86
Concentrates fed	1174	1425	1709
Milk Ave.	11194	13622	13702
Butterfat Ave.	403	482	494

All cows in the herd were injected with Impro after February 1962. By February 1963 the herd average had increased by 2428 lbs. of milk. The % days in milk had also increased by 5% which alone could account for approximately 690 lbs. of milk. Concentrates fed were increased by 251 lbs. per cow which could be responsible for an additional 627 lbs. of milk. These two factors could account for 1317 lbs. of milk from the total of 2428 lbs. increase from 1962 to 1963.

The increase from 1963 to 1964 was only 125 lbs. of milk. The grain fed increased by 284 lbs. per cow which should increase milk by 710 lbs. This indicates that (all other things being equal) Impro had no effect on the next year's production, and also that the herd owner increased grain even though he got no increase in milk yield.

2. Split herd trials.

This data was assembled after the fact and not as a designed trial. Miss Collins told us that cows receiving Impro were those that had previously experienced troubles such as, mastitis, retained placenta, breeding problems, etc., which resulted in lowered production. Normal cows in the same herd were considered as controls. The benefits of Impro were based on changes in production in succeeding lactations by the treated and control groups respectively. Because the treated cows had previous problems, you would expect them to have larger increases than the control cows even if they did not receive Impro. They were almost certain to show large increases.

3. Comparison of first lactation heifers.

A group of first lactation heifers were paired according to their birth dates and one group received Impro while the other group acted as a control. We determined the "proof" of the sires represented by the two groups. Of the 7 Impro cows, four were sired by A.I. proven bulls of exceptional merit. Their collective proof would average a plus 954 lbs. of milk. Of the 9 control cows, only two were sired by proven bulls. One of these bulls has a minus 527 lbs. of milk and the other has a plus proving. Sires alone could account for the observed differences in milk production.

4. Comparison of daughters of a single sire.

Treated and untreated daughters of the same sire were compared. It developed, however, that the treated cows were in one herd and the untreated cows were in another herd. It is impossible to evaluate between herd differences.

We are not saying that Impro has no beneficial effects on milk production. In fact it is our hope that the product will do all that the manufacturer claims. We do say, however, that other circumstances could account for a large portion of the increases in milk yield. There is enough reasonable doubt that we recommend delaying a license until we have an opportunity to evaluate the product.

Title: Evaluation of the effect of routine vaccination with "Impro" on lactation milk yield.

Justification: The Impro Products, Inc. of Waukon, Iowa, has applied to the Veterinary Biologics Division, ARS, for a license to market a compound by the trade name of "Impro." It is claimed that an injection of 50 cc of "Impro" prior (5-10 days) to calving will cause a significant increase in lactation milk production.

They have submitted data that indicates substantial increases in milk yield associated with the use of this compound. The data, however, are open to criticism, due to the lack of planned experimentation.

If the use of this compound will increase milk yield, presumably by increasing the animals natural resistance to infection, its general use should be recommended at the earliest possible date. On the other hand if other factors were responsible for the increases in yield that have been attributed to the use of "Impro", we should not recommend its general distribution.

Objective: To determine whether or not an injection of 50 cc of "Impro" 5-10 days prior to calving will increase milk production.

Plan of Work:

1. Location and number of herds: A number of private dairymen in the vicinity of Beltsville, Maryland, cooperate with the Dairy Cattle Research Branch in various research projects. We will enlist the cooperation of 3 to 5 of these dairies having a total of approximately 500 cows to conduct this project. Selection of the particular dairies will depend on the number of cows in the herd and the competence and interest of the herd managers.

2. Experimental design:
   A. All cows in each herd will be divided into two groups according to the lactation number of their next calving.

   B. First lactation:
      (1) Divide into groups according to sire.
      (2) List each sire group in order of expected calving date.
      (3) Toss a coin to determine the designation of the first animal on each list. Then alternate the remainder of the animals on each sire list to the two treatment groups. These groups will be identified as H-heads and T-tails.

   C. Second and later lactations:
      (1) Divide each lactation group according to month of calving (expected).
      (2) List each group in descending order according to production in their last lactation (305 days).
      (3) Assign to groups H and T as in (3) above.

D. Vaccination of animals: Each animal will receive a 50 cc. subcutaneous injection 5-10 days prior to the expected date of calving. In order to maintain complete experimental control and preclude any possible herdsman interaction, all animals in each herd will receive an injection. The herdsman will be given two sets of coded bottles, one set will contain "Impro" and the other set sterile distilled H_2O, with instructions to inject all animals in group H with one and all animals in group T with the other.

E. Data collection and analysis: Beginning with the first test period after the first animal in each herd calves, all production records of experimental animals will be tabulated. In addition to milk and fat yield taken from the official test sheets, each herdsman will be asked to keep records pertaining to the animal's general health, mastitis incidence, unusual occurrences and reasons for eliminating animals from the herd. These herd records will be collected and tabulated.

All records will be subjected to a periodic analysis in an effort to detect positive results at the earliest possible date. The total time, number, and length of individual records required to detect real differences will vary inversly with the size of the real differences between treatments. Good estimates, however, should be available 6 months after an average of 20 experimental animal per herd calve.

APPENDIX 4
Dr. R. E. Hodgson, AHD

November 1, 1967

Honorable H. R. Gross
House of Representatives

Dear Mr. Gross:

This is in further reply to your letter of October 10 requesting information regarding the licensing of Impro. Your questions are answered in the order listed:

Prior to the issuance of the special license, Impro License No. 258, were you not supplied with official D.H.I.A. actual production records showing the effectiveness of Impro in the licensed 4-State area?

Prior to March 17, 1967, the date of U. S. Veterinary License No. 258 Special, we were supplied with official D.H.I.A. production records from Iowa dairy herds. Production records from the other 3 States were not supplied prior to the issuance of this Special License.

All of the D.H.I.A. production records submitted by the firm were not considered valid in support of the firm's license application. Production records from split herds only -- that is, herds in which part of the animals were treated with Impro and the remainder were untreated controls -- were considered valid. There were 7 herds consisting of 123 dairy cows, of which 55 were treated with Impro, and 68 were left untreated. Production records from the split herds showed an increase in milk production by the treated animals, compared to untreated groups of cows in the same herds. However, our scientists in the Animal Husbandry Research Division pointed out that the treated and untreated cows in these experiments may not have been selected in the most objective manner. Further, these scientists indicated that other factors such as breeding, feed, and percent days in milk can account for increased milk production. In their analysis of the data, they were unable to determine whether the increased milk production was due to treatment with Impro or other factors.

Do you have any official records from this 4 State area disproving the effectiveness of Impro?

We have no official D.H.I.A. records from the 4 State area specifically disproving the effectiveness of Impro.

Hasn't the Impro Company always cooperated in supplying your department with any and all information requested? Such being the case, why have you refused to extend this license?

Impro Products, Inc., earnestly tried to furnish all information and data requested. The applicant, however, placed considerable emphasis on data accumulated from uncontrolled studies which could not be considered valid by the Veterinary Biologics Division. Further, much data were gathered after routine use of the product and were not the result of controlled studies specifically designed to prove the effectiveness of Impro. We refused to extend the applicant's Special License because statistically and scientifically valid experiments conducted by the Agricultural Research Service did not substantiate the claims made by the applicant for his product. These studies include 9 dairy herds consisting of 404 cows, 207 of which were treated with Impro, and 197 left as untreated controls.

With reference to the test conducted by the Animal Husbandry Division, ARS:

What date was the test started?

The first cooperating dairy herd was started on October 3, 1966. The other herds were started during the succeeding 2 weeks.

What date was the test completed?

The test is still in progress in that some of the cows in the trial are still in lactation. All of the cows will complete their lactations in December of this year.

Were Impro Company recommendations on the use of the product followed in the test?

Directions provided by Impro Products, Inc. were followed. Cows were injected approximately 5 - 7 days prior to freshening with 30 cc. of Impro.

What veterinarian had charge of the test?

A veterinarian was not in charge of the test. The 4 major research people involved have Ph.D. degrees in the fields of Microbiology, Physiology, and Statistics. They are competent to conduct this test.

Were milk samples cultured? By whom?

No milk samples were cultured. The Impro product was licensed for the purpose of increased milk production. The purpose of the ARS test was to determine if it accomplished that objective. Culturing of milk samples was considered immaterial.

Were any cows reinjected during lactation because of subnormal production?

No cows were reinjected during the test because no instructions were given to follow such a procedure. Only 1 injection 5 - 7 days prior to freshening was called for.

At the time you refused to extend the Impro license, did you have personal knowledge of:

The number of cows injected with Impro - Date of injection - Date of freshening?

Number of control cows injected - Date of injection - Date of freshening?

Records were kept on each individual cow concerning her date of injection and date of freshening for both the treated and control cows. Records are too extensive to list in this letter, but they are available for review at Beltsville.

Individual cow health evaluation, mastitis incidence, signed by herdsmen according to test plan?

Herdsmen and owners kept records of abnormalities as they occurred. Notes were only made on those cows that were not considered normal. Records such as these kept by dairymen are not very complete.

Are breeding efficiency records available in this test?

These records are available. A summary of these data is as follows:

Treatment	No. of Herds	No. of Cows	No. Pregnant	Services per Conception
Placebo (Saline)	4	151	94	1.84
Whey (Impro)	4	150	104	2.04
Placebo (Normal) Whey)	5	76	56	1.70
Whey (Impro)	5	83/460	50	1.60

There appears to be no significant difference in breeding efficiency between comparative groups from the same herds or composite groups receiving the same treatment from several herds.

Was your evaluation made from actual or projected records?

The evaluation of milk production between the 2 groups of cows was made from both actual and projected records. Results were the same when either kind of record was used.

Your interest in this matter is appreciated, and if we can be of further assistance, please let us know.

Sincerely yours,

J. M. Hejl

J. M. Hejl
Director
Research

cc: Dr. R. E. Hodgson, An./Husbandry Div.

Following are names of scientists who conducted tests at Beltsville, Md.:

J. W. Smith, Ph.D.
Research Animal Scientist (Genetics)
USDA-SEA, FR, NER, BARC
Animal Physiology and Genetics Institute
Building 173, Room 102A
Beltsville, Maryland 20705

C. A. Kiddy, Ph.D.
Research Animal Scientist (Physiologist)
USDA-SEA, FR, NER, BARC, APGI
Reproduction Laboratory
Building 200, Rm. 1
Beltstille, Maryland 20705

R. D. Plowman, Ph.D.
Agricultural Administrator
USDA-SEA, FR, Western Region
Idaho-Montana-Utah Area
Utha State University
UMC 48, Agricultural Science Building
Logan, Utah 84322

W. D. Schultze, Ph.D.
Microbiologist
USDA-SEA, FR, NER, BARC, APGI
Genetics and Management Laboratory
Building 173
Beltsville, Maryland 20705

N. W. Hoover, Jr., M.S.
Supervisory Animal Husbandman
USDA-SEA, FR, NER, BARC
Animal Operations Unit
Building 200, Rm. 20
Beltsville, Maryland 20705

Mr. VOLKMER. I would also like to request that all the original records—not that print—documenting exactly who injected and when they injected each individual herd and the records that were kept as to the effect of it and everything, the original records, handwritten notes, typewritten notes, or whatever they were—I want every bit of it. I do not want just the final thing put out like that [indicating exhibit I].

Dr. BERTRAND. Yes, sir, we will supply that.

[The following is an explanation of materials submitted and held in the subcommittee file:]

EXPLANATION OF ENCLOSED MATERIALS

The first section of enclosed material contains a copy of all lists, notes, and summaries of data in our files which relate to the project on the effect of the routine use of Impro on lactation milk yield. The production records were transcribed from copies of the dairymen's DHIA records borrowed from the University of Maryland and subsequently returned. The information on reproduction and health was transcribed from records maintained by the individual dairymen. Some notes and summaries were discarded over the 10 years since the completion of the study as files were reduced to conserve file space. However, the files transcribed for Congressman Gross in October 1969 reflect all of the raw data available at that time. The data were checked for accurancy and completeness. That is, the data sent to Congressman Gross are an accurate reproduction of the information in our files. In most cases, we went back to the farm in an attempt to get complete answers to all questions, even though our original project was to evaluate milk yield only.

The second section contains 17 appendixes. The following is a brief summary of our efforts to answer the many questions raised by the Impro Company:

1. In an effort to provide information as early as possible, we agreed to provide preliminary summaries during the course of the trial. The first such summary was forwarded to Veterinary Biologics Division (VBD) June 8, 1967. (Appendix 1).

2. Several questions were relayed and answered via phone. We also agreed to prepare a second preliminary summary and provide all detailed data to the company and Congressman H. R. Gross. This information was sent to VBD October 10, 1967. (Appendix 2).

3. Received a copy of letter dated October 10, 1967, from Congressman H. R. Gross with questions regarding trial. (Appendix 3).

4. Answers were provided in a memorandum from Hejl dated November 1, 1967. (Appendix 4).

5. We were informed that VBD had agreed to send our second preliminary report to outside reviewers for evaluation. The report was sent to Dr. Steve Roberts, Cornell University; Dr. Guy Morse, University of Pennsylvania; and Dr. J. E. Legates, North Carolina State University. The copies of their responses are enclosed. (Appendixes 5, 6, and 7).

6. Received letter of December 4, 1967, with list of questions from Mary Collins. (Appendix 8).

7. Provided answers on December 27, 1967. (Appendix 9).

8. Received a copy of letter from Congressman Gross dated August 6 1969, requesting all detail on Impro trial. (Appendix 10).

9. Forwarded copy of all detailed data with covering memorandum dated October 6, 1969. In the process of assembling this data we went back to the farms to get additional information that has not been included and rechecked all data. (Appendix 11).

10. Received request for additional information from Congressman Gross dated December 30, 1969. (Appendix 12).

11. Provided information in memo dated January 13, 1970. (Appendix 13).

12. The company used the detailed data to select some of the cows in the Beltsville herd and printed an advertising flyer showing that Impro was benficial in the Beltsville herd. (Appendix 14).

13. Received request for additional records dated September 25, 1970. (Appendix 15). We responded on October 22, 1970 but do not now have file copy of what was sent. We believe we sent them a copy of the complete detailed record set provided Congressman Gross.

During the course of the study, we made repeated requests for an opportunity to discuss the work with Miss Collins, any scientists involved in testing products for the company, and members of Congressman Gross's staff. In answering questions, we endeavored to use the best or most complete data available.

Appendix 16 contains the results of the "Beltsville field trial". Original data for this report are in Appendix 17.

Mr. ROSE. Do you gentlemen have any other questions before we go to vote on the floor?

[Recess taken.]

Mr. ROSE. I would like to excuse for the moment the witnesses at the table and ask them to have a seat in the audience.

At this time I will ask Mr. J. B. Cordaro, Food Group Manager, Office of Technology Assessment, and Dr. Walter Wilcox, Consultant to the Office of Technology Assessment, to come forward.

You may proceed.

STATEMENT OF J. B. CORDARO, FOOD GROUP MANAGER, U.S. CONGRESS, OFFICE OF TECHNOLOGY ASSESSMENT

Mr. CORDARO. Thank you very much, Mr. Chairman. I appreciate the opportunity to be with you today.

Dr. Wilcox and I are here today to give you some of the early indications of the results of our OTA study on the use of chemicals and drugs in animal feeds.

OTA was asked by the Senate Agriculture Committee to review the decision that Commissioner Don Kennedy, Commissioner of the Food and Drug Administration has made regarding the use of certain antibiotics used at the subtherapeutic level for animal feed. We will be presenting a comprehensive report to the Congress for use in the 96th Congress. The report is in its final draft stage and is being reviewed.

Mr. ROSE. We appreciate your coming and we look forward to your report.

I wrote you on August 17 asking you to address in your report the implications of production costs if there is a transfer from the current system for health maintenance of dairy cattle and poultry to an antibody system of treatment, if this might occur. Do you have any indication of that?

Mr. CORDARO. We do not have the specific information here. What we do have are the preliminary results of the economic consequences of the various scenarios on the removal of the use of the antibiotics. This is what Dr. Wilcox is prepared to address now, Mr. Chairman, and this is what Dr. Russell Peterson, OTA's director indicated in his letter of August 30 to you would be provided.

Mr. ROSE. Thank you very much.

Dr. Wilcox, could you give us just a summary of that, please?

STATEMENT OF WALTER WILCOX, CONSULTANT TO THE OFFICE OF TECHNOLOGY ASSESSMENT

Dr. WILCOX. This is a paper prepared as part of our overall assessment by Professor Headley of the University of Missouri. He had four scenarios that he used in running through a simulation model estimating the effects, in the first place, of banning DES with no effective substitute and carrying it through for 10 years—what that would do to beef and cattle supplies and prices.

Then the second one was the banning of tetracyclines and penicillin with no substitutes. He carried that through for 10 years.

Then the third one would be the banning of nitrofurans and sulfa. Again he carried it through for 10 years.

Then he tried all four of those, leaving out DES. Finally, he tried it if all of these were removed with no substitutes. In other words, all antibiotics, nitrofurans, sulfas, and DES would be left out. He estimated the effect on supplies and prices. This was the way he went about it.

He came to the conclusion that overall retail meat prices, if DES were banned with no substitute, would be 6 to 7 percent higher the first year or so. After adjustments in the industry, they would drop down so that the retail meat prices would average about 5 percent higher if there were no substitutes and DES was banned.

As you know, there are substitutes and we have cut down very sharply on the use of DES. We are using other hormones in animal feeding at the present time which largely take its place.

Going on to the second scenario where you only ban the tetracyclines and penicillins, we came out with not as much adverse effect on meat prices but very substantial effect on poultry prices. It would be about 5 percent. Broiler prices would be some 7 percent higher as an average over the 10-year period.

Tetracyclines and penicillins primarily are used in hog and poultry production and, to a lesser extent, in cattle production, so there was not much adverse effect on cattle production and cattle prices, except to the extent that there would be smaller competitive supplies of pork and chicken if you were banning those two things.

Then if you ban the nitrofurans and the sulfas, you get a substantially greater price effect, particularly on poultry. For example, the wholesale price of broilers might be expected to be as much as 30 percent higher than it would be otherwise. Turkey prices again would be 25 to 30 percent higher than they would be otherwise. Meat prices would be 7 or 8 percent higher than otherwise.

In the case of banning all of them, it was up slightly more than that. There was roughly a 10-percent increase in retail prices of meat. I have figures here as high as 50-percent increase in the wholesale price of broilers and 36, 37, or 38 percent higher prices for turkeys, if you ban tetracyclines, nitrofurans, penicillin, and sulfas.

I might say Professor Headley used all the information that was available in the Department of Agriculture, the Food and Drug Administration, and the independent research that has been carried on at Iowa State University and other places in building his model.

If you ban all of these, he comes up with 15- to 20-percent increase in meat prices and pretty close to 50-percent increase in the farm turkey price and the wholesale price of broilers.

In terms of per capita increase in costs, that first scenario, just banning DES, would result in $7 to $8 per capita increase in meat costs. The second scenario would be $5.70. The third scenario would increase per capita costs by about $12. The fourth scenario would increase per capita costs about $19. The last one would increase them about $22.

That is very briefly the summary of the results that he got. I have his complete paper. If you would like to have it put into the record, I would be happy to do that.

[The paper referred to, "Economic Aspects of Drug and Chemical Feed Additives," is held in the subcommittee file.]

Mr. ROSE. Thank you very much, Dr. Wilcox.

Are there any questions from members of the subcommittee?

Mr. VOLKMER. I would like to ask Dr. Wilcox and/or Mr. Cordaro a question.

Is your report going to involve any antibodies or just antibiotics?

Dr. WILCOX. It will involve just drugs and chemicals.

Mr. VOLKMER. Thank you.

Mr. ROSE. Gentlemen, we want to thank you. We look forward to your final report.

Mr. CORDARO. Thank you very much, Congressman Rose.

Mr. ROSE. I would like to ask Ms. Collins, Dr. Campbell, and Mr. Schmidt, to come back to the witness table briefly.

I understand that Dr. Campbell is a veterinarian in Lewiston, Minn., and Mr. Schmidt is a dairy farmer in Sturgeon Bay, Wis.

Dr. Campbell, could you relate to us your experience with the antibody compounds in your practice?

Dr. CAMPBELL. Antibiotic compounds?

Mr. ROSE. Antibodies.

Dr. CAMPBELL. Briefly, I would say we have been using the product ever since it has been available, which would be in the vicinity of 11 or 12 years.

Ms. COLLINS. Twelve years.

Dr. CAMPBELL. We have had a variety of experiences with it. Probably our most common use of it would be in subacute or chronic cases of mastitis. Our second most important use would have been in a mastitis-metritis syndrome in sows. Probably our third most use would have been in a calf scour syndrome where se see sudden death.

Mr. ROSE. What is your general impression of the product that Ms. Collins has produced?

Dr. CAMPBELL. I would say it is a very effective tool in our trade, the veterinary business. At the moment, I would hate to be without it because we do run into a lot of antibiotic-resistant bugs. We have done an extensive amount of culture and sensitivity testing for the past 12 years, since we have had this tool at our disposal. When we run into various resistant bacteria, we have been fortunate enough to be able to revert back to some of the antibodies that have been produced and see a successful treatment.

Mr. ROSE. Have you ever observed any ill effects or any effects that could be attributed as ill effects to the use of antibodies, either in the treated animal or in the handlers or those administering antibodies?

Dr. CAMPBELL. No, I have had no problem with antigalactic shock. We have given as much as three bottles I.V. in a cow. That would be a dose level up quite a bit over recommended doses.

Mr. ROSE. Mr. Schmidt, has your experience paralleled that of Dr. Campbell's?

Mr. SCHMIDT. It does, Mr. Chairman.

Mr. ROSE. Do you have any observations you could share with us about the use of antibody compounds in your herd?

Mr. SCHMIDT. My main observation would be that, from where I stand today, I really do not know how I would farm without it.

We started 4 years ago with cows that were extremely sick of mastitis, many types of mastitis. Over a period of 4 years they have come to a point where we have been receiving quality awards for quality

milk from our cooperative. We have cows that have a high-level of health, as has been witnessed by tests which were recently run by the Dairy Herd Improvement Association, as is stated in the document which I have presented here.

Somatic cell count, which is a measure of mastitic activity in milk, has been run on our herd. The State average for that particular test in the State of Wisconsin for August of 1978, shows that over 15 percent of all cows in the State of Wisconsin have a high degree of mastitis in their milk. Only 65 percent have what would be considered to be completely clean milk. For our herd, we have only 2 percent which are considered to be excessive mastitic and over 87 percent that are completely clean.

My strongest feeling is that I do not know what I would use. We have used antibiotics in the past and I have had to dump excessive amounts of milk. We have found antibiotics in many cases completely ineffective, whereas this product, both as a specific product for a specific type of bacteria, and as a general product—that is, there are different types of this product available—seems to have, and I know it has, great benefit to the animals.

Mr. ROSE. Mr. Schmidt, do you have a statement that you prepared for today?

Mr. SCHMIDT. I have a statement, yes. It is a history of our farm and our experience. It is available for the record. You have copies, I am sure.

Mr. ROSE. Thank you.

[The prepared statement of Mr. Schmidt follows:]

STATEMENT OF WILLIAM SCHMIDT

DAIRY FARMER FROM STURGEON BAY, WISCONSIN,

My name is William J. Schmidt. I am a dairy farmer from Sturgeon Bay, Wisconsin. I grew up on the farm that I am now farming.

Before my present involvement in the dairy industry, I was a computer analyst and nuclear field engineer with General Electric Company. I am a mechanical engineer with a masters degree from Marquette University in mechanical and nuclear engineering.

I returned to the dairy business in 1971 and have been involved in a two family partnership since 1973.

This Committee is asking: Can we produce quality milk without antibiotics?

Four years ago this month, my brother and I were asking questions pertaining to our survival as dairy farmers. We had to ask ourselves three important questions:

1. With the amount of mastitis and sickness in our herd, could we continue to be dairy farmers?

2. With the amount of mastitis and sickness in our herd, could we produce milk which had the quality to market?

3. With the amount of mastitis and sickness in our herd, could we produce the quantity required to make it economically feasible for us to farm?

We needed something to help rid us of this mastitis so we could again have healthy cows and quality milk. As many other farmers have, we were desperately searching to find ways to put herd health and economics together.

In October, 1974, we took samples of milk from each of our cows and sent them to a laboratory to be cultured. The culture report indicated that we had 41 out of 90 cows with pseudomonas mastitis. We also had cows with types of mastitis such as staph, strep ag, ecoli, and others. At the time of the culture samples, we were using large amounts of antibiotics and dumping up to 1500 lbs. of milk per day (down the drain). We had been using almost every type of antibiotic available to us over the counter and from our veterinarian. In fact, we had difficulty finding a cow with good enough milk to use for our own (raw) consumption. Even our young calves became ill from drinking the milk and many died. When our veterinarian heard of the culture report, he said the only solution was to sell all the ill cows, because pseudomonas mastitis could not be cured with any drugs on the present market.

Our situation was not a happy one. We searched magazines, spoke to as many persons involved with cows as we could, made contacts across the country, and visited other "successful" farms. It was at this time that we became aware of an antibody product, produced by Impro Products of Waukon, Iowa.

We began to use this product and had very pleasant results. Our cows responded to the treatment and their health began to return. We no longer have large numbers of cows with psudomonas mastitis.

We no longer have cows dying from toxic poisoning assoc-

iated with ecoli mastitis. We also no longer dump large quantities of milk due to antibiotic residue. From that time to the present, we have used few antibiotics because we have found them less effective. We must say it has not completely eliminated mastitis from our herd, which now numbers over 100, but we are marketing significantly better milk than four years ago. We are also marketing more milk per cow than we ever have. Our cows show their health through quantity and quality, as is evidenced by the increase in our production and quality milk awards we have received from our cooperative the last two years. In 1976, we ranked ninth in our county on a quality milk rating. During the 1977 year we ranked fourth in our county.

In August 1978, we had all of our cows tested on the somatic cell count test. The Dairy Herd Improvement Association does this testing and scores each herd relative to the state average. A somatic cell count above 800,000 indicates an infection. A count of 400,000-800,000 is a caution area. Cows below 400,000 are considered healthy, or uninfected. The August 1978, Wisconsin state average was as follows:

15% over 800,000
20% between 400,000 and 800,000
65% under 400,000

Our scores were:

2% over 800,000
11% between 400,000 and 800,00
87% under 400,000

We realize many factors are involved in animal health, but our experience has shown us that an antibody product has helped us significantly to produce milk of good quality.

Mr. ROSE. I would like to ask Drs. Crawford and Bertrand to respond to some questions.

Would it be possible for us to get you, either jointly or severally, to take another look at these tests that were conducted at Beltsville with an eye toward possibly conducting them again?

Dr. BERTRAND. Mr. Chairman, we would be delighted to do that from a USDA point of view. May I suggest that we look at the data one more time? Then we can consider running additional tests if it seems to be appropriate.

Mr. ROSE. Thank you very much.

Dr. CRAWFORD. Mr. Chairman, I would be happy to do so. As you know, this is not FDA's purview, but I would be delighted to work with Dr. Bertrand in any way he sees fit.

[The following letter was received:]

UNITED STATES DEPARTMENT OF AGRICULTURE
SCIENCE AND EDUCATION ADMINISTRATION

OFFICE OF THE DIRECTOR
WASHINGTON, D.C. 20250

OCT 20 1978

Honorable Charles Rose
Chairman
Subcommittee on Dairy
and Poultry
Committee on Agriculture
House of Representatives
Washington, D.C. 20515

Dear Mr. Chairman:

Pursuant to your request at the September 27th hearing of the Dairy and Poultry Subcommittee on the use of antibodies in animal health management for poultry and dairy cattle, we have developed a procedure to review the results of the tests on Impro Whey Antibody Blend conducted at the U.S. Department of Agriculture Research Center at Beltsville, Maryland.

We plan to review and evaluate both the data from the Beltsville tests and the data which Impro Products, Inc., has submitted to the Animal, Plant and Health Inspection Service (APHIS) of the Department of Agriculture. We intend to evaluate only the effect of the injection of Impro Whey Antibody on milk production under standard herd management conditions. Two scientists, who have not been involved in Federal government tests of Impro Whey Antibody Blend have been selected to conduct the actual review and evaluation of the Beltsville and the Impro data. Their names are:

Fred Kingma, D.V.M.
Associate Director
Scientific Services
Bureau of Veterinary Medicine
HFV-2
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857
301-443-3450

C. John Maré, D.V.M.
Professor and Head
Department of Research and
Science of Animal Virology
University of Arizona
Tucson, Arizona 85721
602-626-2355

Both men are veterinarians. Dr. Kingma's specialty is pharmacology, and Dr. Maré's specialties are immunology and virology.

Following their examination of the data, they will write a report of their findings. We will review the report and make a determination as to whether the Department of Agriculture should retest the Impro Whey Antibody Blend. Subsequently, we will inform you of our decision and the reasons for the decision. We estimate that 60 days will be required for the scientific review, the preparation of the report, and our response to you.

We hope this proposal is agreeable to you and look forward to continuing to work with you and the others Members of your Subcommittee.

Sincerely,

ANSON R. BERTRAND
Director
Science and Education
USDA

LES CRAWFORD, DVM
Director
Bureau of Veterinary Medicine
FDA

Mr. ROSE. Dr. Crawford, I understand you have just come to the Department as the new Director of the Bureau of Veterinary Medicine.

Dr. CRAWFORD. Yes, sir.

Mr. ROSE. Being fresh from the public sector, could you tell us what is the opinion generally—and don't spare the words—of antibodies as a form of treatment in veterinarian medicine? Has the American Veterinary Medical Association ever taken a position on antibodies?

Dr. CRAWFORD. Not insofar as I know.

Speaking of antibodies just generally, I think the feeling of the profession is that they are of short-term benefit, if I may not spare the words and say the way it is.

Mr. ROSE. I understand from my conversations and what I have read about this—and you correct me if I am wrong—obviously antibodies are something that Mother Nature produces, has produced, and will continue to produce with or without license from the Food and Drug Administration. [Laughter.]

Ms. COLLINS. That is correct.

Mr. ROSE. All that Mary Collins and Impro Products have done is to patent for a rather limited period of time a process by which freshening cows produce antibodies in such a way that they can be transferred to other animal organisms. Is that correct, Ms. Collins?

Ms. COLLINS. To other animals, yes, and people.

Mr. ROSE. Ms. Collins, what is your answer, if you have one, to the statement that short-term usages are possible here?

Ms. COLLINS. I am sure that this is right in antibodies relating to blood serum. This is what Dr. Crawford was discussing—antibodies relating to blood serum.

Our problem is that this is a different type of product. This immunocompetent factor cannot be measured.

There is not a doubt in my mind that it is longer term, but why no one knows. Do we help that animal overcome the infection and her own antibody system operates at a higher peak? These are questions in immunology that will be answered in the future, I hope while I am still around.

When you work this many years and do this much observation on these animals and on these people, it is entirely different than any concept that any of us have ever worked with before. That has contributed to our difficulty, but I do not see why it should.

Mr. ROSE. Dr. Campbell, do you have any observations you would like to make in regard to what she just said?

Dr. CAMPBELL. Yes. I think each animal's immunological system or the ability to produce antibodies varies. In the treatment of mastitis we will get animals that we treat sometimes that will clear up for the rest of the lactation. We will get animals occasionally that will break back in a month's time. We have occasional animals that will break back in about 5 to 7 days' time. We can retreat them with a heavier dose and retreat them again and clear up the case of mastitis. The animal may stay clear for the rest of the lactation.

When you start dealing with some of staph and antibiotics, they frequently break back. You get what is known as an old chronic staph cow that the majority of veterinarians would recommend selling to get the source of infection out of the heard.

Mr. ROSE. Congressman Hagedorn.

Mr. HAGEDORN. I have a couple of questions.

First, Dr. Crawford, would you briefly describe your previous practice? Were you in private practice before you accepted this position? What has been your background?

Dr. CRAWFORD. I have been in private practice and also in academia at the University of Georgia. I spent most of my career there. I have also been in the industry.

Mr. HAGEDORN. You have had practical, on-the-farm experience, so to speak?

Dr. CRAWFORD. Yes, I have a lot of on-the-farm experience.

Mr. HAGEDORN. Quite often we have people who come in who don't have any.

Mr. VOLKMER. Would the gentleman yield on that point?

Mr. HAGEDORN. Yes.

Mr. VOLKMER. Has any of that been with dairy herds?

Dr. CRAWFORD. Yes. I was raised on a dairy farm.

Mr. VOLKMER. Then you know what mastitis is?

Dr. CRAWFORD. Yes. That is one of the reasons I am here today.

Mr. HAGEDORN. I have a question for Dr. Campbell.

Do you use this Impro product on a one-shot basis, or is it administered over a period of time on a continuing basis? How is it used?

Dr. CAMPBELL. Our most use has been what we would call subacute cases of mastitis, where the farmer has a cow, she is not really sick, she is still eating, but she has a quarter that is showing flakey milk on the strainer pad or on the teacup when he would test her out before milking. He is faced with the problem: Do I treat this cow with antibiotics and dump milk for 72 hours or longer, if it works, or do I use the Impro product and not have to dump any milk? If you match up the right Impro product with the right bacteria in the udder, she will clear right up in 24 hours.

Mr. HAGEDORN. And you don't have to treat it any more?

Dr. CAMPBELL. No, depending upon the bacteria and response to the treatment.

Mr. HAGEDORN. Do you look at this as a last-ditch effort or do you use this as a first-type of treatment?

Dr. CAMPBELL. We definitely do not look at it as a last-ditch effort. We have a lot of Impro that has been dispensed out of our clinic and used in these minor flareups where it does not generally affect the health of the cow. It is a firstline of defense quite often.

Mr. HAGEDORN. That is very interesting.

I don't have any other questions, Mr. Chairman.

Mr. ROSE. Congressman Volkmer.

Mr. VOLKMER. I would like to ask a few questions.

Is it used by injection?

Dr. CAMPBELL. Yes.

Mr. VOLKMER. Injection in the udder?

Dr. CAMPBELL. No. This has been used mainly as a subcutaneous injection. We have some dairy farmers who use it as a routine preventiod for organisms that may have lodged in the udder during the dry cow period and not flared up. They will routinely shoot the cows within 10 days of freshening, right down the row every cow in the herd.

35-830 O - 79 - 5

Actually the product is used in a variety of ways.

Mr. VOLKMER. Then it is not by any intravenous or any other method?

Dr. CAMPBELL. It can be in severe, acute cases of mastitis, yes.

Mr. VOLKMER. I don't quite understand. Are you presently having difficulties with FDA in the use of this?

Mr. ROSE. I think Ms. Collins could best respond to that.

Ms. COLLINS. We are having difficulty. There seems to be utter confusion about what we are and where we belong. However, our real difficulty started with the Beltsville test when we had a license issued.

Mr. VOLKMER. Let's ignore that. Right now you are still being able to market it or not market it?

Ms. COLLINS. No. We are just marketing it on an intrastate basis.

Mr. VOLKMER. Intrastate or interstate?

Ms. COLLINS. Intrastate.

Mr. VOLKMER. Within the State only?

Ms. COLLINS. That is right.

We had to set up facilities. We operate in four States, which is why these half a million dairy cows that have been injected and on the Impro program are all in the Midwest: Iowa, Wisconsin, Minnesota, and Illinois.

Mr. VOLKMER. As to all those, approximately how many herds would you be serving at the present time?

Ms. COLLINS. It would be difficult. It would be in the hundreds. I could get some pretty reasonable figures.

Mr. VOLKMER. How long have you been using this product now in these herds?

Ms. COLLINS. We started 12 years ago working on a product for dairy calves. We went from that to pigs. Then we went to dairy cattle.

I would say the last few years there have been 400,000 or 500,000 dairy cows injected. Figuring that on a 50-herd average, we are probably looking at least at 700 or 800 herds.

Would you think that was reasonable, Dr. Campbell?

Dr. CAMPBELL. I would say probably just in our practice alone during the course of a year we will have Impro used in 75 to 100 herds.

Mr. VOLKMER. What I am trying to get at is, if anyone wants to examine any animals, they could examine those.

Ms. COLLINS. Absolutely. These dairy people with whom we work are interested in production and in producing top-flight milk.

Mr. VOLKMER. Have there been any problems with the milk itself as a result of this? Have there been any harmful effects?

Ms. COLLINS. Absolutely none. All milk has antibodies in it. It could not be foreign because we produce this from the udder of a cow. We extract it from milk. This milk is no different from any other milk by anything you can measure, which is why you have to have very tight controls in the production of the milk.

Mr. VOLKMER. What you are telling us basically is that your problem arises from the fact that you have run into something and you know what it does but you don't know why it does it. Nobody else knows why.

Ms. COLLINS. Yes. Nobody can measure it.

We have a product, which you will become aware of, Dr. Crawford. We have food products for the animals. They were under Food and Drug. Food and Drug made their inspections and consulted with us on labeling and everything. In August we got a letter from the Division of Biologics saying, "We have now decided your foods are biologics and you are in violation of the law."

Mr. VOLKMER. In other words, because there is not perhaps sufficient—I don't want to say intelligence but maybe I should say imagination—imagination within the Department——

Ms. COLLINS. Certainly there is lack of vision.

Mr. VOLKMER. Lack of vision or imagination. They cannot see it. There may be something there that they have not experienced yet or read about yet.

Ms. COLLINS. That is right.

We had one Federal veterinarian tell us that maybe only God is going to be able to classify this product, and I think he is right. Although it would be difficult to conceive, I could conceive where we could be not under either Food and Drug or the Division of Biologics.

Mr. VOLKMER. Mr. Schmidt, do you use this product?

Mr. SCHMIDT. Yes, we do. We use it continually.

Mr. VOLKMER. How many years have you used it?

Mr. SCHMIDT. Since October 1974.

Mr. VOLKMER. You have used it 4 years then?

Mr. SCHMIDT. Yes, we have.

Mr. VOLKMER. With satisfaction?

Mr. SCHMIDT. With satisfaction.

Mr. VOLKMER. That sounds better than the scientists to me.

Mr. SCHMIDT. Let me comment, if I may.

I don't think that people should go away with an impression, or that you should get an impression, that it is some kind of a miracle drug.

Mr. VOLKMER. I agree with that. I think it has limited use and a valid use.

Mr. SCHMIDT. Yes, it does, sir.

Mr. VOLKMER. I don't think there are any warranties being put out by anybody that it is a wonder drug or anything like that, and I don't consider it that. I do consider it as a possible use for those intelligent people who are in the dairy industry who are basically businessmen. If they want to make a judgment that they would rather use that than an antibiotic, then they should have the right to use it rather than an antibiotic, knowing its limitations.

Mr. SCHMIDT. Yes. That is an excellent statement.

Mr. VOLKMER. The Government doesn't have to protect them from something that is not hurting them really.

Mr. ROSE. Thank you very much. That was a very helpful exchange. I think that underscores my interest here. That is to shed light and not heat. I believe that heat will be generated by those who feel that their various domains are being threatened or that some system of knowledge that they have previously held to might be subject to some alteration to make room for a different phenomenon.

The real bottom line for this hearing is to see that the agencies that, on the one hand, are telling us that antibiotics in use in society may

pose the theoretical possibility of creating supposed resistances that are harmful to humans, should not at the same time be making it difficult for organizations such as Impro and people such as Ms. Collins and her company to market wherever they wish to do so a product that, from what we have seen, has not been given a fair shake.

I very much appreciate Dr. Bertrand's statement that he will gather the data; that they will make it available to us; that they will retest this product; and that we will be able to see those results. Congressman Volkmer.

Mr. VOLKMER. Dr. Bertrand, you have pointed out in your statement the large amounts that are used for allocation for research, approximately $11,800,000. Is that correct?

Dr. BERTRAND. Yes.

Mr. VOLKMER. Non-Federal funds from cooperating institutions is approximately $9 million. The total is $21,719,000. How much of that research is on antibodies?

Dr. BERTRAND. I could not answer that specifically, sir.

Mr. VOLKMER. Can you advise us by letter?

Dr. BERTRAND. I certainly will.

Mr. VOLKMER. I would like to know how much is being done on antibiotics.

[The following information was submitted:]

On September 8, 1978, Dr. Richard Alsmeyer, Cooperative Research, Science and Education Administration (SEA–CR), provided the Subcommittee on Dairy and Poultry with a list of antibody and immune response research projects recorded in the CRIS system. He also provided the Subcommittee with the dollar value of the Fiscal Year 1977 Cooperative Research funds ($1,598,551) and research effort by the States ($11,422,829) which is comprised primarily of non-Federal funds. The $1,598,551 is included in the total. In his testimony of September 27th before the Subcommittee, Dr. Bertrand stated that the Department had approximately $11,895,000 in research (of which antibody research is part) and that cooperating institutions had committed $9,824,000 to this research, making a total of $21,719,000 being spent in this area of research in the United States. Most of the Department's immune research ($10,297,000) is conducted by the Agricultural Research unit of the Science and Education Administration (SEA–AR) and the remainder (approximately $1,598,000) is funded by SEA–CR and used by State cooperators for immune research.

The attached table shows the breakdown of the funding for antibody and antibiotic research for SEA–AR, SEA–CR, and for the Department's non-Federal cooperators.

A breakdown of funding for research on antibodies and antibiotics by funding agency follows:

FUNDING ON ANTIBODIES AND ANTIBIOTICS
Source of Funds (in $ thousands)

	SEA-AR*	SEA-CR**	Cooperators	Total
Antibodies a/	5,148	799	4,912	10,859 b/
Antibiotics	small c/	135	540	+675

a/ Approximately half of the research on immunity is on antibiodies

b/ Total funds on immunity is $21,719,000

c/ Some research not closely identified on areas such as "Monensin" for coccidiosis in poultry, "Rumensin" for improved ruminant nutrition, and "Tetracyclines" for Anaplasmosis. Most research in this area is conducted by pharmaceutical companies.

* SEA-AR = Science and Education Administration-Agricultural Research

** SEA-CR = Science and Education Administration-Cooperative Research

Antibody research includes the maintenance of healthy herds.

The Department and its cooperators have about $10.9 million centered on antibody research. This includes the maintenance of healthy herds and flocks through the prevention and treatment of disease with antibodies, the duration and protective value of antibodies produced by vaccination, the development of diagnostic tests to identify antibodies of specific diseases, characterization of antibody proteins, characterization of antigen-antibody reactions, mechanism of protective action of antibodies, interaction of antibodies and other immunity mechanisms in disease prevention, the role of antibody in auto immune diseases, and other research to clarify the nature and use of antibodies in the diagnosis, prevention, and control of livestock and poultry diseases.

Antibiotic research is being conducted by a number of State agricultural experiment stations supported in part by Hatch funds administered through Cooperative Research, Science and Education Administration. The majority of this research centers on the use of

35-830 O - 79 - 6

antibiotics in livestock and poultry health. Due to regulatory concerns, very little new research is being conducted on the low level use of antibiotics as growth promotants; however, a number of States (12) are evaluating nonantibiotic, growth-promoting substances as replacements for antibiotics. Cooperative Research is allocating about $135,000 for this research and the States about $540,000 in non-Federal funds.

Animal health uses of antibiotics are being studied as follows:

Mastitis - Nine States are evaluating the efficacy of various antibiotics to eradicate the disease duing the dry-cow period. Studies are determining minimum effective dosages, methods for minimizing milk contamination, and effect of therapy on susceptibility to future infection.

Shipping Fever - Eight States are evaluating efficacy of antibiotics as preventatives of shipping fever in cattle and as treatment for the acute disease. Resistance of causative organisms is under study and rate of dissemination of these resistant strains is being determined.

Salmonellosis - Four States are studying means of controlling salmonella infection in poultry with antibiotics and determining methods of overcoming antibiotic resistance.

Poultry Respiratory Diseases - Three States are studying methods for eradicating mycoplasma by antibiotic treatment of eggs prior to hatching.

Atrophic Rhinitis Fowl Cholera Pink Eye Swine Dysentery	Four States are working on these problems to develop satisfactory means of control with antibiotics. The potential for antibiotics resistance is being assessed and methods sought to overcome this resistance.

Growth Promotion in Livestock and Poultry - Three States are studying effect of low level administration of antibiotics on growth and bacterial flora of the intestine. The resulting antibiotic resistance of intestinal bacteria is being determined.

UNITED STATES DEPARTMENT OF AGRICULTURE
SCIENCE AND EDUCATION ADMINISTRATION

OFFICE OF THE DIRECTOR
WASHINGTON, D.C. 20250

NOV 3 1978

Honorable Harold L. Volkmer
Subcommittee on Dairy
and Poultry
Committee on Agriculture
House of Representatives
Washington, D.C. 20515

Dear Congressman Volkmer:

This is in response to your request at the September 27th hearing for information on the use of antibodies in animal health maintenance for poultry and dairy cattle. You asked, "Non-Federal funds from cooperating institutions is approximately $9 million. The total is $21,719,000. How much of that research is on antibodies?"

The Department and its cooperators have about $10.9 million centered on antibody research. This includes the maintenance of healthy herds and flocks through the prevention and treatment of disease with antibodies, the duration and protective value of antibodies produced by vaccination, the development of diagnostic tests to identify antibodies of specific diseases, characterization of antibody proteins, characterization of antigen-antibody reactions, mechanism of protective action of antibodies, interaction of antibodies and other immunity mechanisms in disease prevention, the role of antibody in auto immune diseases, and other research to clarify the nature and use of antibodies in the diagnosis, prevention, and control of livestock and poultry diseases.

Subsequently, you said, "I would like to know how much is being done on antibiotics."

Research on antibiotics is being conducted by a number of State Agricultural Experiment Stations supported in part by Hatch funds administered through Cooperative Research, Science and Education Administration. The majority of this research centers on the use of antibiotics in livestock and poultry health. Due to regulatory concerns, very little new research is being conducted on the low level use of antibiotics as growth promotants; however, a number of States (12) are evaluating nonantibiotic, growth-promoting substances as replacements for antibiotics. Cooperative Research is allocating about $135,000 to this research and the States about $540,000 in non-Federal funds.

Honorable Harold L. Volkmer

Animal health uses of antibiotics are being studied as follows:

Mastitis - Nine States are evaluating the efficacy of various antibiotics to eradicate the disease during the dry-cow period. Studies are determining minimum effective dosages, methods for minimizing milk contamination, and effect of therapy on susceptibility to future infection.

Shipping Fever - Eight States are evaluating the efficacy of antibiotics as preventatives of shipping fever in cattle and as treatment for the acute disease. Resistance of causative organisms is under study and rate of dissemination of these resistant strains is being determined.

Salmonellosis - Four States are studying means of controlling salmonella infection in poultry with antibiotics and determining methods of overcoming antibiotic resistance.

Poultry Respiratory Diseases - Three States are studying methods for eradicating mycoplasma by antibiotic treatment of eggs prior to hatching.

Atrophic Rhinitis
Fowl Cholera
Pink Eye
Swine Dysentery

Four States are working on these problems to develop satisfactory means of control with antibiotics. The potential for antibiotics resistance is being assessed and methods sought to overcome this resistance.

Growth Promotion in Livestock and Poultry - Three States are studying the effect of low level administration of antibiotics on growth and bacterial flora of the intestine. The resulting antibiotic resistance of intestinal bacteria is being determined.

If you have any further questions, I would be delighted to obtain additional information for you.

Sincerely,

Ralph G. McCarthy

for ANSON R. BERTRAND
Director
Science and Education

cc:
Congressman Rose
Carol Forbes

Mr. ROSE. Dr. Crawford and Dr. Bertrand, wouldn't you surmise that we are probably not doing any research on antibodies as a health system in animal health maintenance?

Dr. BERTRAND. Again, I would rather reply with an accurate statement later, if I may.

Mr. ROSE. Thank you very much.

[The following information was submitted:]

All the research conducted on antibodies by the Department and its cooperators is directed towards maintenance of animal health.

Mr. ROSE. Ms. Collins, Dr. Campbell, and Mr. Schmidt, we will excuse you for a minute.

Ms. COLLINS. Thank you very much. It has been a pleasure.

Mr. ROSE. Thank you.

Our next witness is Mr. Lloyd Massey, master of the North Carolina State Grange, representing the National Grange.

Mr. Massey, I appreciate your presence.

Do you have a statement?

Mr. MASSEY. Yes, I do.

[The prepared statement of Mr. Massey follows:]

STATEMENT BY

LLOYD M. MASSEY

MASTER, NORTH CAROLINA STATE GRANGE

MR. CHAIRMAN AND MEMBERS OF THE COMMITTEE:

I AM LLOYD M. MASSEY, MASTER OF THE NORTH CAROLINA STATE GRANGE WITH HOME OFFICE IN GREENSBORO, N. C.

I APPEAR HERE ON BEHALF OF THE NATIONAL AND STATE GRANGE, REPRESENTING HALF A MILLION MEMBERS ACROSS THE COUNTRY.

I WISH TO THANK THE CHAIRMAN AND MEMBERS OF THIS COMMITTEE FOR HOLDING THIS HEARING THAT YOU MAY BE AWARE OF THE EXTENT TO WHICH SCIENTISTS AND GOVERNMENT HAVE EXPLORED THE USE OF ANTIBIOTICS AS A TOOL FOR MAINTAINING HEALTHY FOOD-PRODUCING ANIMALS.

THE GRANGE BELIEVES THE FAMILY FARM IS THE MOST EFFICIENT AND ECONOMIC WAY TO PRODUCE THE FOOD FOR OUR PEOPLE AND HELP FEED THE PEOPLE AROUND THE WORLD. PRODUCTIVITY ON U. S. FARMS HAS REACHED A PLATEAU. NEW KNOWLEDGE MUST BE GENERATED SO THAT AGRICULTURAL GROWTH CAN KEEP PACE WITH POPULATION GAINS. OVER THE PAST FIFTEEN YEARS THERE HAS BEEN A DRAMATIC INCREASE IN FARM PRODUCTION. MILK YIELDS INCREASED 50%; RED MEAT IN HOGS ROSE 11%; AND FEED EFFICIENCY IN BROILERS INCREASED 18%.

WE DO NOT BELIEVE THE VITAL, SUCCESSFUL AND PROFITABLE LIVESTOCK AND POULTRY OPERATION IN NORTH CAROLINA AND THE NATION COULD HAVE ACHIEVED THESE INCREASES WITHOUT THE USE OF ANTIBIOTICS IN ANIMAL FEEDS. IN 1977, FARM RECEIPTS FROM THE SALE OF LIVESTOCK AND POULTRY AMOUNTED TO 1.03 BILLION DOLLARS, REPRESENTING 40% OF THE TOTAL CASH FARM INCOME IN NORTH CAROLINA, AND I AM SURE THIS REFLECTS THE SAME ACROSS THE NATION.

TETRACYCLINES IN FEED HAVE BEEN USED TO HELP PRODUCE OVER 100 BILLION ANIMALS IN THE UNITED STATES DURING THE PAST 27 YEARS WITH NO ADVERSE EFFECT ON THE ANIMAL, THE HUMAN FEEDING THE ANIMAL OR THE HUMANS CONSUMING THE ANIMAL PRODUCTS. THERE IS NO EVIDENCE THAT THE FEEDING OF TETRACYCLINES TO FOOD ANIMALS HAS EVER RESULTED IN THE TRANSFER OF ANTIBIOTIC RESISTANCE FROM ANIMAL TO MAN.

ON JANUARY 24, 1977, THE NATIONAL ADVISORY FOOD AND DRUG COMMITTEE

RECOMMENDED THE CONTINUED USE OF TETRACYCLINES FOR LIVESTOCK AND POULTRY FEEDS IN AN UNCHANGED FASHION.

THE COUNCIL FOR AGRICULTURAL SCIENCE AND TECHNOLOGY TASK FORCE REPORT NUMBER 22, PREPARED AT THE REQUEST OF CONGRESSMAN L. H. FOUNTAIN RECOMMENDED THE CONTINUED USE OF TETRACYCLINES IN LIVESTOCY AND POULTRY FEEDS.

THERE IS NOW AN IN-DEPTH REVIEW OF THE ANTIBIOTIC SITUATION AT THE UNIVERSITY OF KENTUCKY UNDER THE DIRECTION OF THE TASK FORCE WITH DR. VIRGIL HAYS, HEAD OF ANIMAL SCIENCE.

THE AMERICAN DAIRY SCIENCE ASSOCIATION, AMERICAN SOCIETY OF ANIMAL SCIENCE, AND THE POULTRY SCIENCE ASSOCIATION ALL HAVE FEED ADDITIVE COMMITTEES WHICH MAINTAIN A CONTINUING REVIEW OF THE SAFETY AND EFFICACY OF FEED ADDITIVE AND ANTIBIOTICS. THEY HAVE NOT FOUND EVIDENCE TO SUPPORT ANY ACTION THAT WOULD CHANGE THE PROCEDURES WHICH ARE NOW IN USE IN REGARD TO TETRACYCLINES AND THEY RECOMMEND THAT ITS CONTINUED USE BE UNCHANGED.

NORTH CAROLINA AND THE NATION WOULD BE HIT PARTICULARLY HARD IF CERTAIN ANTIBIOTICS COULD BE USED ONLY ON THE ORDER OF LICENSED VETERINARIANS, SINCE VETERINARIANS DO NOT EVEN RESIDE IN 18 OUT OF 100 COUNTIES IN THE STATE. I AM SURE THIS SITUATION EXISTS IN OTHER AREAS OF THE NATION AS WELL.

AS I STATED IN THE BEGINNING, THE GRANGE BELIEVES IN THE FAMILY FARM AND ITS PLACE IN OUR ECONOMIC SYSTEM. IF PROPOSED REQUIREMENT (THAT THE FEEDING OF ANTIBIOTICS BE PLACED UNDER THE CONTROL OF LICENSED VETERINARIANS), IS INITIATED, IT WOULD WORK AGAINST THE SMALL INDEPENDENT LIVESTOCK PRODUCER. MANY LARGE LIVESTOCK AND POULTRY PRODUCERS HAVE LICENSED VETERINARIANS ON THEIR PAYROLL WHO COULD PRESCRIBE ANTIBIOTICS AS WELL: WHEREAS THE SMALL PRODUCERS WOULD NEED TO WORK THROUGH A PRACTICING VETERINARIAN WHO MIGHT BE MILES AWAY.

I ASK THAT THIS STATEMENT BE MADE A PART OF THE HEARING RECORD.

I WISH TO THANK YOU, MR. CHAIRMAN, FOR THE LEADERSHIP YOU ARE GIVING AMERICAN AGRICULTURE. YOU AND MEMBERS OF YOUR COMMITTEE WILL GIVE, I AM SURE, DUE CONSIDERATION TO THE ISSUE AT HAND AND I HOPE YOU WILL USE YOUR INFLUENCE ON BEHALF OF THE LIVESTOCK PRODUCERS OF OUR NATION.

Mr. ROSE. Mr. Massey, I agree completely with what you have said. I appreciate your having the courage to come here today and tell us this. It is what some people might regard as a controversial hearing. I agree with your statement.

I wish the National Milk Producers Federation had not decided to pull out of these hearings but had come and given us their opinion. We think that all parts of the dairy industry and the drug industry need to be aware of all of these problems and not afraid to look at anybody's solution. That is the way we have always done business in this country, and I guess we will continue.

Thank you, Mr. Massey.

These hearings are concluded for today.

[Whereupon, at 12:35 p.m., the subcommittee recessed, to reconvene at the call of the Chair.]

[The prepared statement submitted by Ms. Collins follows:]

STATEMENT OF MARY COLLINS

IMPRO PRODUCTS, WAUKON, IOWA,

BEFORE THE SUBCOMMITTEE ON DAIRY AND POULTRY,

COMMITTEE ON AGRICULTURE,

UNITED STATES HOUSE OF REPRESENTATIVES

Mr. Chairman and members of the Subcommittee:

My name is Mary Collins. I am the Corporate Secretary-Treasurer of Impro Products, Inc. of Waukon, Iowa and I appear before this Sub-Committee on behalf of that corporation. I would like to express my sincere appreciation to you, Mr. Chairman, and the other members of the Sub-Committee, and its staff, for the opportunity of making such an appearance at this hearing.

Impro Products, Inc. is a Minnesota Corporation having its principal place of business at Waukon, Iowa. It was organized in 1962 by members of the Collins family and it is primarily still a closely held corporation, though there are non-family stockholders as well. It was organized and exists today for the purpose of engaging in research, development and production of milk whey products for use in the animal health industry.

As suggested in your notice of this meeting our firm has been an innovator of a treatment system for stimulating antibody development in animals. A bit of the background as to how and why we got involved in this activity plus some of the obstacles and results achieved are as follows:

For the last twenty years we have been involved in developing and field testing an antibody product produced in the udder of a cow. We've been privileged to work with dairymen in the Midwest in aiding them to produce a top quality milk product without the routine use of antibiotics in their day to day operation. I would like to share with you the story of the development of this product.

In the late 1940's my family was raising pigs on our farm with all the attendant problems of pig farmers everywhere. After a sow lays on one or two baby pigs, and baby pig scours hit, the farmer is lucky to raise five or six pigs from a litter of ten. My brother Bob, who was an engineer in Alaska, came home to help me shape things up. He designed and patented an individual house called a Pigloo, a round farrowing house. (Exhibit A). The first pigs we farrowed in Pigloos were in the winter of 1951. We never lost a baby pig from being laid on, and these pigs weighed about ten pounds more at weaning than the pigs in the central house with the same breeding and feed. Instead of weaning seven or eight pigs, we were weaning ten or eleven. When you add ten pounds more per pig, then pig farming starts to be profitable and enjoyable.

Now began the work of finding out, "Why the difference?" I thought it was the sunshine and fresh air. When it was below zero and the sun was shining, these baby pigs were out in the pen and then they would come in, nurse and sleep as if dead. However, this explanation wasn't complicated enough for my brother Jim, a genetics student, and he was right.

We were putting the sows in the Pigloos a week or ten days before farrowing so they would settle down and make a nest. What we didn't realize was that we were exposing the sow to all the bacteria in a confined area, and she was developing antibody protection for her baby pigs. The baby pigs

were confined to this same area and had this antibody protection constantly available to them through her milk. About this time we were contacted by Dr. George Young from the University of Nebraska. He had developed specific pathogen free pigs and was using Pigloos to farrow his first generation gilts. Dr. Young performed an experiment that confirmed our thinking. He took the white blood count on two litters of pigs every two hours for 24 hours and it remained constant. He then built a run-way between the two Pigloos and let the baby pigs run back and forth, exposing them to bacteria for which their mothers did not have protection. In twelve hours their white count had doubled which indicated a challenge to their system, although there were no visible signs of illness. If a person with abdominal pain was in the hospital and this happened, he could be subjected to exploratory surgery to find the cause. This shows the extreme effect of cross infection in baby pigs.

Dr. Young's work showed that this protection phenomenon occurred through nature when a sow is confined to a limited area and is isolated from other sows and litters. At this same time my brother Jim, who was a graduate student at the University of Minnesota, was working with Dr. William E. Peterson, a dairy scientist, who was doing basic work in producing specific protection in the udder of a dairy cow, relative to human problems. Dr. Peterson came to us and asked us to take over his work. We felt Dr. Young's and Dr. Peterson's works were interrelated. At this point, having over 7,000 pigloo units out and business being good, we decided to undertake Dr. Peterson's project.

To make my points, I must relate to you incidents from both our human research and our animal research, although from a point of time they overlapped. First I want to go into the human area.

Dr. Peterson had done some work with humans that showed promise. We went to Notre Dame and consulted with Dr. James Reyneir of Lobund Institute who was to give us much advice and counsel during the remaining years of his life. Perhaps he helped us so much because he had spent his life doing something

that was not scientifically possible; that is, raising animals to produce generation after generation with no germs--a germ-free animal which turned out to be a major contribution to medical research.

Since staph 80 and 81, or hospital staph, was causing such a problem, we produced a product to cover that bacteria. Dr. Reynier suggested that we use the entire product, including the fat, for oral absorption. He felt the fat might have something to do with preparing the gut for the antibodies to go through, or they might even ride piggy-back on the fat. This was not a very palatable product since we had to freeze the milk for storage and the fat would not go back into suspension. However, this didn't last long. Our family physician knew we had this hospital staph product because my sister was going to drink some before she went into the hospital to have a baby. Dr. Jeffries called one afternoon and said he had a patient very sick with Staph 80 and 81 pneumonia. He wanted to try some of our product. The patient was a female, in her early 50's, a diabetic. The bacteria showed a resistance to all antibiotics tested except two--both of which had kicked the diabetes completely out of control and had to be discontinued. I told him what Dr. Reynier had said and asked him if she could drink whole milk.

He said, "Hell, no. She's sick. She can't drink anything and we can't tube milk. It would coagulate in the tube. Take the fat off, the solids out, and bring me some at the hospital. And hurry up!"

IMMUNOCOMPETENT FACTOR

It took us from four o'clock in the afternoon until eleven o'clock at night to defrost the milk and process it to whey. I took what we had to the hospital that night. About nine-thirty the next morning, the doctor called for more. Dr. Jeffries reported the patient showed some clinical

improvement at 48 hours and at 72 hours the lab could not culture the staph and the patient made a normal recovery. This product, Staph 80 and 81, was administered either tubed or orally to eight patients by three physicians, pretty generally following this pattern. However, this first patient was the only one not also on antibiotic therapy. These results contradict the age old theory that an antibody cannot be assimilated through the G.I. tract after 48 hours following birth. This seemed arbitrary to me anyhow, as no other facility with which one is born is taken away from everybody at precisely the same time. I always felt that nursed babies had less problems at four months and six months than bottle fed babies. I happen to think nursing is a two-way street -- the baby gets milk and infuses the mother with any germs in the baby's mouth; then gets the protection back at future nursings.

An outstanding physician who was following our work and giving us counsel felt that Staph 80 and 81 was not a good product for conducting tests. The patients were too critical and everything had to be used to try to save lives, thus clouding results. He suggested we work on urinary tract infections. These were deep seated and they do not respond well to antibiotics. Infection tended to recur but did not tend to be critical or go into septicima. One factor that intrigued us was that the four most prominent bacteria in dairy cattle -- Pseudomonas, Proteus, E. Coli and A.A. were also the most often isolated bacteria in human urinary tract problems. We could culture the urine on daily intervals. So we picked up urinary tract bacteria from a hospital in Minnesota and Dr. Menolasino picked up some at a hospital in Chicago. During the summer of 1963, vaccines were made, cows infused, products produced, and research programs planned.

On September 21, 1963, a little four-year old girl named Peggy from our town was badly burned. One Sunday morning she came down to the kitchen when her parents were in church and her older sister was sleeping. Peggy decided to fix popcorn for breakfast. She shoved a chair up to the gas stove, turned on the burner and reached into the cupboard for the popcorn. Her pajamas caught on fire. Typically she ran outside screaming. When her sister caught her, she was burned over 60 percent of her body; 37 percent of this was third degree. After a few days in the local hospital, she was transferred to a Minnesota hospital. It is fantastic what can be done for shock and kidney function with burned patients but not for the infection. Sometime in early October we learned that Peggy was on the critical list with staph. We were just sick. We had a niece her age and they looked enough alike to be sisters. I knew that when you are doing research with any physician, you never ask for your product to be used outside of controlled research. We also knew every aspect of our products was being put down by some influential men from the land grant colleges. We were close to broke but I decided to call her dad at the hospital. I had gone to school with him. I asked Bill if Peggy had Staph 80 and 81 and he said, "Yes and she is terribly sick."

I said to him, "You won't understand this, but we have a product that has worked in some of these cases. You can tell your physician that he can call me if he wants to." He didn't call. The next afternoon Bill was home and called me over to his store. He said when the physician came in the night before, he told him they had the staph under control. That morning, before Bill returned home, the physician told Bill and Marge that Peggy now had a blood disease that no drug would treat. I thought perhaps it was an irreversible blood condition similar to acute anemia which sometime occurs after a

combination of drugs have to be used. I told him I was sorry and was just leaving when he said, "It is pseudo something."

I said, "not pseudomonas?" and he replied, "Yes. That's it."

I said, " If you promise me you will never tell a soul, I will call a physician friend of mine to see if it would be possible to try our pseudomonas product."

Unlike our staph product, this product had never been used on a critical case. The origin of the bacteria used to produce the product was from urinary tract infections and not pseudomonas from a burn infection. I knew we might not be able to do it but we would try.

"Please," he said.

I called this physician about 5:15. When I told my story, he said, "Mary, if they referred to this infection as a blood disease that means blood septecima (poisoning), and she can't live."

I said, "I know."

He said, "We have to try. I will contact her physician and pediatrician and offer them some pseudomonas product."

Her temperature had peaked at 105 every day for 21 days. She was on I.V. They would have to tube it and couldn't tell how much she would retain. They started at eight o'clock that night and in 24 hours she retained almost a quart. In 48 hours she seemed clinically to change, and in 72 hours they could no longer culture pseudomonas from the blood. The physicians reported to us, to their knowledge, Peggy was the first person to recover from pseudomonas septicemia. They continued her on the pseudomonas product and it was March before the open burn areas were free of pseudomonas.

Next came the grafting for Peggy. On pseudomonas patients grafts tend not to take. If 50 per cent of the graft didn't take, it would be critical

because of additional open areas. The first graft took between 90 and 95 percent and on April 1 Peggy came home for the first time. I have a picture of her. Peggy had to return many times for surgery but is now a lovely 19 year old college sophomore.

I took your time to review these two human cases to point out:

1. the activity in neither of these products could be measured by any technique presently available to science, and

2. this product had to be absorbed through the G.I. Tract of a four year old little girl and a fifty year old woman. Neither of these characteristics exist under current biologic concepts so we might well presume our Impro Products are not of a biologic nature. For this reason we have chosen to designate our product as containing an immunocompetent factor.

In the animal field pursuing Dr. Peterson's work, we decided to experiment with baby calves because once a baby calf is sick the death loss is extremely high. Instead of trying to find out what anybody else thought caused this high death loss in baby calves, we decided to find out from the calves.

I went to Chicago and recruited one of the top microbiologists in the area, Dr. N.G. Menolasino, to work with us. Dr. Menolasino felt enough good work had been done on this theory of producing this protection in the udder of a cow to be worth pursuing. If we followed our plan we would know in a year if it were practical.

So back I went to Iowa and the next week we went to the sale barn and bought four 3-day old baby calves. These calves had been exposed to the bacteria on the farm, in the truck, and at the sale barn. We took them to the farm and put them together in a pen. You better believe me, we never had to

challenge a calf to make it sick. In twenty-four hours, the ears would be down, the nose would run and then the cough started. Diarrhea would follow and, usually, by the 5th or 6th day they would be down. Just before the calf died, we would have the veterinarian electrocute it.

He would post the calf and send specimens of lung, liver, intestine, brain, heart, blood, spleen, kidney and other specimens he thought significant to Dr. Menolasino. Dr. Menolasino would identify the bacteria and note which bacteria, in his opinion, caused the death. We continued this work through the winter and probably posted 200 calves. We picked up pseudomonas, E. Coli, A.A., Proteus, some Staph and Strep, and it formed a definite pattern. Dr. Menolasino then made killed vaccines and we infused separate cows with the vaccines at weekly intervals, at least three weeks before freshening. After the cow freshened, we saved the milk, removed the fat and solids, took the whey product containing immunocompetent factors, pasteurized it, added a preservative, bottled it and were now ready to use it.

By this time another winter was approaching. We were very fortunate to have three excellent veterinarians in our home town who were looking for answers to the problems they found in the field. We asked them to take this product when they had a calf that was down, inject 20 cc and let us know the results. This was the most dramatic product we ever worked with. If the product used covered the problem which it did in a high percentage of the cases, the calf would be up drinking and nosing around for food in two or three hours. They were saw legged and weak but better. If we failed to cover the problem, the calf would go right ahead and die on schedule just like our penned calves. The veterinarian would then post and send specimens to Dr. Menolasino who would identify the bacteria and make a vaccine to add to our spectrum. Little by little we expanded the coverage spectrum of our product until it reached that point where it was covering a majority of the problems.

35-830 O - 79 - 7

This is off the record but it is humorous. A local veterinarian had a client who was experiencing severe calf losses. He asked the dairyman if he would sacrifice a calf so he could post it and send in specimens for analysis. When the dairyman agreed, the calf was electrocuted and specimens were submitted. The state lab report that followed listed the cause of death--struck by lightning.

The next thing we tackled was baby pig problems. This was much easier now that we had a pattern established and the product was ready for testing in about six months. The bacterial pattern was similar to calves, but less pnemounia and more coliforms.

This product seemed effective in reducing baby pig losses but one day we got a call from a farmer in Monona, Iowa, who was losing a percentage of baby pigs from each litter. As he had Pigloos and was injecting the baby pigs with our product, theoretically, he shouldn't be having problems. However, at about three days of age, these baby pigs just shriveled up and died. It almost looked like TGE. The veterinarian posted several pigs and sent them to Dr. Merolasino who was unable to isolate any pathogens. More were posted with the same results. Dr. Menolasino thought it must be toxins in the milk. We asked the farmer if he would butcher some sows so we could send specimens to the lab. He did and we picked up Proteus and E. Coli in the reproductive tract and milk glands of the sow. After he injected the sows with these two products, there was a decided improvement in the herd. Here was a very valuable lesson for us, because it taught us to ask the animal what the problem was and take the straight systemic approach in handling it. The problem showed up in the milk, but part of it was the reproductive tract.

After observing the disadvantages of young calves being put together in the same pens, it was obvious some work had to be done on a calf housing

system. We went back to nature. What does a mother cow do with her young if you give her a chance? She hides her calf so well that it is very difficult to find it.

My brother Bob designed a building like a box 8 feet long, 4 feet wide, and 4 feet high, twice as deep as it is wide so that it operates like a bottle. The oxygen remains the same as the outside at 20.5% without a draft. This has a definite effect on the metabolism of the calf. If you drop oxygen 1 point to 19.5%, the rate of metabolism of the calf drops 5 percent. Since warm moist air travels automatically to cold dry air mechanically without a draft if you do not restrict it, this was the perfect housing system for baby calves. He called his building a "Calfloo" (Exhibit B) because of using the same air control system he had used in pigloos. The name "Calfloo" was copyrighted in 1958.

We made these calfloo blueprints available to the industry at no cost, and they have been so successful that the Extension men from the University of Wisconsin and South Dakota now think they invented them, only they call them hutches. That is what I call real success when anybody in the Extension Service thinks we have done something right.

The housing systems designed by Bob Collins and made available to agriculture, including Pigloos, Calfloos and finishing hutches for growing pigs have been a major contribution to the agricultural industry.

Our next undertaking was dairy cows with mastitis. We asked several veterinarians to take milk cultures from cows with mastitis before they gave them antibiotics. I remember the first culture we received was an E. Coli, which shouldn't have been in the udder of a cow. When the veterinarian lost a downer cow, he would post her and send specimens to our lab where we picked up pathogens in lungs, liver, and reproductive tract that we felt were contributing to the problem.

We worked with about eighteen veterinarians, testing our product for mastitis. The results were encouraging though not as clear cut as in our previous work. One observation was that many of the cows that were injected with our product went on and produced more milk than they had ever produced before.

Dr. Bob Sander, a veterinarian we worked with, said, "You know, so many of these problems happen after calving. Let's pick a herd and inject every cow before she calves. We might eliminate some of these problems and the cows might produce more milk."

We selected Ken Kerndt's herd. It took about a year and a half to inject each cow as she freshened and have her complete her 305 day lactation. Also, if any cow dropped in milk production during her lactation she was reinjected. At the end of the year, the average cow in the herd produced 1560 lbs. of milk over its previous lactation. Our product didn't eliminate all the problems in the herd and it never will. As long as you have livestock, you are going to have problems and the only way to eliminate them completely is to sell the cows. As a matter of fact that is exactly what some of the colleges recommend to dairy farmers with problem herds.

The difference it made in yearly income to this dairyman was about $2,450.00 more milk income. Milk sold at $3.30 per hundred in 1965. His product cost, about $418.00, resulted in a net increase in his income of over $2,000. Today, with milk at $10.50, his increased herd income would be over $6,900. Mr. Kerndt's milk quality was excellent.

We also started to accumulate similar data from other herds, and, elated with results, we took off for Washington to get a license for the product. These were the records we took with us (Exhibit C)

You can see we did not go with testimonials about what a dairyman or veterinarian thought, but with official dairy herd improvement records where the milk was weighed and calculated by a third person every month.

Our application was submitted to FDA citing a claim of increased milk production. After six weeks, it was decided we did not fit under them and the application was sent on to USDA, Division of Biologics, to see if our product belonged under them. They decided we were a biologic and then our problems really began. The only standards they had were for blood serum.

This decision was very disappointing to use because we felt that we should not be classified as a biologic.

It was obvious from the data that was being accumulated in the field that dairymen using our product were increasing their milk production and eliminating the use of antibiotics in their milk production programs. USDA decided to give us a two-year license for the United States in order to acquire large amounts of field data. (Exhibit D) We would also have this time to try to develop a more accurate and sensitive test for evaluation. As soon as this announcement was made, the ARS, which is part of the Extension Service, got into the act to see if they could keep the special license from being issued.

This gave us great cause for concern because of our previous relationship with our extension veterinarian from Iowa, Dr. John Herrick, from Iowa State University. He had written us several times in 1959 about the interesting work we were doing. He came to see us and said we should have an article published in a scientific journal on our calf work, and he would help us get it published. He proceeded to get an article published in MODERN VETERINARY PRACTICE. We were elated. Dr. Herrick maintained his friendly, interested attitude until the spring of 1962 when he came to our office and during a

private conversation between Dr. Herrick and myself, he told me he had all kinds of connections and would like $100 a month as a consultant to help in promoting our product and getting our license. The checks were to be sent to his home at 202 S. Hazel, Ames, Iowa. Since no one else was present, the only proof I have is what he did before this date and after. I told him my brothers were in this business too, and I could not make the decision alone. We discussed this and felt when such great people as Dr. Reynier and some of the physicians we worked with had put their scientific reputation on the line to advise and help us, there was no way we would ruin our future with payola. We felt if this product did what it looked like it would, nobody could stop it. If it didn't, no one could make it go. The future would be decided in the market place. This was a very costly decision.

At this time we marketed our product only through veterinarians and wanted to continue this practice. Later I was to find Dr. Herrick had a close relationship with many of the major drug companies. His association with many of the top men in the U.S.D.A. was affecting the future of our products. In the next few years he spent much time trying to eliminate us from the market place. Using his association with Iowa Secretary of Agriculture, and the State Veterinarian, he not only destroyed our creditability with veterinarians, which forced us to go directly to the farmer, but he also attempted to get our business in Iowa closed. Only through the efforts of a state Senator, who used our product in his herd, were we able to avoid this. Dr. Herrick, through Dr. Geyer of the U.S.D.A., obtained information given to the Division of Biologics when he knew we had filed an application there. I have copies of letters to substantiate these statements. On July 15, 1966, Dr. Peacock sent a notice to all Extension Departments announcing that a two-year license was being issued to us. On August 16, 1966, we received a telephone call from Dr. Davidson of the Division of Biologics who told us they had been

contacted by the Agricultural Research Service of Beltsville saying they wanted to run a test on our product. He never recalled this happening before. On August 30, at the request of Biologics, I went to Washington to meet with Dr. Davidson and personnel from Beltsville regarding the test. When we returned to Hyattsville, Maryland, Dr. Peacock received a call from Dr. Plowman of ARS begging him not to issue a license to us until they could run this test for six months. I told them no one could evaluate this in six months on increased milk production as it had taken us a year and a half. That night I decided to ask for a meeting with Dr. Hejl and told him about my experience with Dr. Herrick, as I felt this was now becoming the MAJOR ISSUE regarding our license.

Dr. Hejl remarked, "that explains one thing. At an Extension Veterinarian meeting that I addressed about a new product, Dr. Herrick came up to me and said, 'Out in Iowa we don't want Impro licensed.'" Dr. Hejl said he wasn't about to discuss our product there but he wondered what Dr. Herrick knew that his department didn't know, so he sent Dr. Davidson back to Iowa to do some checking. In spite of this conversation, we received a letter from Dr. Peacock written to us on September 6th, telling us to bring 450 bottles of our product to Washington so Beltsville could conduct the test. (Exhibit E) On September 23rd, we were in Washington with the product and Dr. Plowman informed us that he had returned from a meeting held the previous week in Ames and had found out all about Impro.

I said, "I can tell you who was there--Dr. Herrick and Donald Voelker." He acknowledged that and added that Dr. Packer was also there. Even with that cheery bit of news, we had no choice except to let these so-called scientific men conduct the test used to deliberately sabatoge our product, or fold the tent on our business. The test was to start on October 6, 1966. From that day on,

the attitude toward us changed in the Divison of Biologics. With the exception of Dr. Graham Davidson and in the field, Dr. Tamoglia who always came with an interested and helpful attitude, we received no help. The attitude was "maybe we'll give you a temporary license." Finally on the following March 17, 1967, a special license for six months for four states was issued with the assurance that it would be renewed because in six months it would be impossible to accumulate field data. This was a far cry from the original announcement of the previous July 15th that we were being issued a two-year license. (Exhibit F).

On July 19, 1967, we were invited to present a program on our product at a Veterinary meeting at Galesville, Wisconsin. There were some fifteen veterinarians and their wives present. Dr. Wayne Burch, an Extension Veterinarian from the University of Wisconsin, was in attendance. He kept interrupting my presentation and finally made this announcement, "I called all over the United States to find out about this product and yesterday Dr. Herrick told me the product was no G.D. good and their license is going to be cancelled." He advised the veterinarians to take a wait and see attitude. It was very embarrassing for everyone and the veterinarian who had invited us told him to shut up and apologized for the incident.

I called Dr. Davidson the next morning and asked him it it were true that our license was being cancelled and he said, "No, don't worry." They had no report from Beltsville and the renewal was quite routine. Dr. Burch of Extension knew more about the Department of Biologics than Dr. Davidson, who was employed there, for on September 27th, we were notified that our license was not being renewed because preliminary reports from Beltsville showed no milk increase.

Following the incident at Galesville, one of the medical men on our

advisory board told us to check with Wisconsin and Minnesota and to consider setting up intrastate operations. If they had that much power, we would be physically and financially drained trying to accomplish anything. We followed his advice and by expending much energy and money accomplished this.

We then set out to accumulate as much evidence on efficacy as possible. This was not testimonial type evidence but official D.H.I.A. records. We had to face the fact that our license was not renewed because of the "scientific work at Beltsville." Back I went to Washington--probably my fifteenth trip to the Department of Biologics-- and asked for the names of the herds used in the Test. Dr. Peacock wasn't going to give them to me but Dr. Davidson insisted I was entitled to them. I rented a car and spent two days in Maryland calling on these herd owners. Every dairyman was nice to me except one. I asked one dairyman who had injected the cows. He said, "I injected some, my herdsman injected some, and a guy from Beltsville injected some." I asked to see the records and a strange look came over his face. He didn't know who kept the records. I was appalled.

I went back to Washington, stopped to see Congressman Gross, told him my story and said, "If I can't get those work sheets, we are out of business." He was very kind and assured me he would try. After several months he got them, and it was worse than we dreamed possible.

With the 460 cows in the Beltsville test, the conclusion was given that the product was worthless and was so alleged in the Scientific Journals. The license to operate interstate was cancelled on these conclusions. Furthermore, it questioned the credibility of any dairyman who had used this product or furnished records.

When one takes the protocol submitted by Beltsville to the USDA for the test and checks it against the report of the actual work submitted (Exhibit G) to

Congressman Gross, it becomes clear that this test, conducted by J.W. Smith, Ph.D., and N.W. Hooven, Jr., M.S. was used to deliberately sabatoge our future.

Let's take a look at what actually happened in the Beltsville test.

Of the 460 animals included in the test:

1. ONLY SIXTY of the test animals were injected according to the protocol.

2. ONLY FORTY EIGHTof the controls were injected according to the protocol.

The Impro injected cows produced 14,830 lbs. of milk for the lactation period; the control cows produced 13,809 lbs. of milk. The treated cows showed a 1,021 pound advantage over the controls thus confirming that the product was effective.

The sloppiness in the conduct of this test was too evident to be attributed to chance. Outright deceit is obvious. The letter of instruction from Dr. Peacock asking us to furnish the product for the test was written on September 6, 1966. The product was personally delivered to Dr. Peacock's office on September 23, 1966.

NINE COWS were injected nineteen days BEFORE THE PRODUCT WAS DELIVERED to start the test, and FIVE COWS were injected eighteen days BEFORE THE PRODUCT WAS DELIVERED for the scientists from Beltsville! This goes beyond sloppy work. Outright deceit is obvious.

According to their protocol the first calf heifers were to be split according to sires (which is the only way you could do it), and was so reported in their scientific publications. The heifers on the Beltsville farm, selected according to protocol, showed a 2,231 lb. of milk advantage over the heifers in the control group. (Exhibit H) When we pointed this out, we were accused of selecting data.

We took the Gross Report to W.A.R.F. Institute at Madison, Wisconsin, for review. (Exhibit I) They reported that, instead of the animals being injected five to seven days before the anticipated calving date as falsely reported in their scientific publications, the truth was they were injected from as early as forty-two days previous to calving and up to seven days after calving. I am sure that there is not a dairyman in the United States who does not know when a cow has calved!

On with their plans--this prestigious group of scientists presented this infamous report at the American Dairy Science Association's annual meeting on June 24, 1969, in Minneapolis, Minnesota. So now the lie is available to the dairy science people at all of the Universities. Next, on July 25, 1969, this report was submitted to the American Veterinary Medical Journal and subsequently published. (Exhibit J) So now the lie had been given to the veterinarians.

Why was negative data so hurridly published in these two prestigious journals? Once a paper is published in an affluent scientific journal, regardless of a retraction or falseness of the data, the negative effect is never fully erased from the mind of the scientific establishment. Innocent veterinarians and dairy people have been misled. There is nothing one can do but try to overcome the damage with truth.

It is now the fall of 1967. Our special license has been cancelled on the preliminary data from the infamous Beltsville test. (Exhibit K) Back we go to the Division of Biologics to object to the manner in which the test has been conducted. Dr. Hejl says he has submitted a complete assembly of our prelicensing data and the AHD's data was prepared and sent to Professor S.J. Roberts, Cornell University, Professor G.E. Morse, University of Pennsylvania, and Professor J.E. Legates, North Carolina State University.

Independently, each of them arrived at the same general conclusions. The firm's data lacked proper experimental design to avoid bias and possibly erroneous conclusions. Statistical analysis of these results would have little meaning and significance. Data from the AHD was properly controlled in contrast to the firm's experiments and demonstrated no significant effect on production levels or breeding efficiency. They also agreed that this license should not be reissued.

Since our meeting with Dr. Hejl took place on October 11, 1967, and the Gross report was not made available until November 1969, I can only assume that the conclusions had to be based on the false information that was later published. We have never been able to get this information from the Division of Biologics or the people that conducted the test but I have now submitted the Gross report to Professor Roberts and Professor Legates and am now awaiting their scientific evaluation of this work.

We now contacted the State officials in Iowa, Wisconsin, and Minnesota, and went through the back-breaking work of acquiring property for processing offices, available herds for production, and getting our business in operation on an intrastate basis. The only thing that made this worthwhile was the reaction of so many fine dairymen to having an alternative to the use of antibiotics in milk production. Antibodies have made a major contribution and will always be necessary to fulfill a need in the field of agriculture.

We are submitting statements and data from sixteen herds covering the use of whey with IMMUNOCOMPETENT factors in 5,432 lactations. (Exhibit L) If we want 10,000 or 20,000 lactations they are available. When you have that many herds producing that much good quality milk using no antibiotics except on sick cows, the question of whether this can be accomplished is not germane to the discussion - it is being done.

At this time I would like to note that we take a holistic approach to the dairy herd as we do to individual animals. When we work with a dairyman, we suggest that he check his milking machine, check his water sources for bacteria and nitrates, raise his heifers in calfloos and use the best management possible.

We also have food supplement products containing immunocompetent factors now registered in forty states. They are under the jurisdiction of Food and Drug Administration and they have continuously made inspections. Since February 6, 1975, they have made nine official inspections. However, on July 24th, we were informed by letter that our foods are now considered Biologics. (Exhibit M) This certainly indicates the state of utter confusion on their part that exists regarding our products.

Most scientists think that, unless you can measure something, it doesn't exist. They couldn't measure the IGA component in blood until 1957 but it had been there doing its work since the creation of the world. We have a product that at present cannot be measured by man. In a way, it is much the same gift of nature as electricity. To this day they only know what electricity is by what it does. They can produce it, ship it, store it and use it but nobody knows what it is. The phenomona is recorded 600 years before Christ when a Greek Philosopher rubbed a piece of amber with a piece of cloth and observed that the amber then attracted bits of feathers and the pith of plants. The real advances were made in the 1800's, of course, by Edison. But remember, that electricity cannot be weighed or measured except by what it does, and electrons cannot be seen even with the microscope developed using them. However, if electricity could not be used until it could be seen or measured, we would be stumbling around in a pretty dark world.

Finally, let's consider Vitamin C, so important to life.

A Portuguese Navigator once lost 100 out of 160 men to scurvey. On the other hand, an English navigator gave his sailors lime juice to drink every day with good results. The situation was so critical that in 1795 the English Navy furnished a daily ration of lime juice to every sailor to provide Vitamin C for all their men at sea. In 1927, ascorbic acid was identified in the adrenal gland of an ox and named Vitamin C. One other of nature's great gifts was given a name. For 202 years the efficacy of Vitamin C was known by observation--now it had been identified.

For seventeen years the immunocompetent factor in our product has been known by efficacy and observation but if it cannot be used until it can be measured, we are refusing another one of nature's great gifts at a time when American Agriculture is on its knees because of the indiscriminate use of antibiotics promoted by every land grant college and drug company in the U.S. The American dairyman is being sold the idea that he cannot produce food without the use of potent drugs. How sad and untrue. The government has acknowledged the safety and purity of our product. The market place has acknowledged the efficacy of the product.

We came before this committee today with confidence that you people can guide us through this planned maize of confusion so this viable system can be made available to the livestock producers of America and not be lost because of its simplicity. Thank you.

(Exhibits referred to are held in the subcommittee file.)

○