History

of the

U. S. Food and Drug Administration

Interviewee: Dr. C.D. VanHouweling

Interviewer: Ronald T. Ottes

Date: June 18, 1990

Place: Pella, Ia

DEED OF GIFT

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C. D. VanHouweling, D.V.M. M.S.

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INTRODUCTION

This is a transcript of a taped oral history interview, one of a series conducted by Robert G. Porter, Fred L. Lofsvold and Ronald T. Ottes, retired employees of the U.S. Food and Drug Administration. The interviews are with persons, whose recollections may serve to augment the written record. It is hoped that these narratives of things past will serve as one source along with written and pictorial source materials, for present and future researchers. The tapes and transcripts will become a part of the collection of the National Library of Medicine.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

TAPE INDEX SHEET

CASSETTE NUMBER(S) 1,2

GENERAL TOPIC OF INTERVIEW: History of The Food and Drug Administration

DATE: June 18, 1990 PLACE: Pella, Iowa LENGTH: 100 minutes

INTERVIEWEE	INTERVIEWER
NAME: Dr. C.D. VanHouweling	NAME: Ronald T. Ottes
ADDRESS: [redacted]	ADDRESS: U.S. Food and Drug Adm.

FDA SERVICE DATES: FROM 1967 TO 1979 RETIRED? Yes

TITLE: Director, Bureau of Veterinary Medicine
(If retired, title of last FDA position)

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RO: This is another in a series of FDA oral history recordings. Today we're interviewing Dr. C.D. VanHouweling, retired director of the Bureau of Veterinary Medicine, currently known as the Center of Veterinary Medicine. The interview is being held in Pella, Iowa. The date is June 18, 1990. I'm Ronald Ottes.

Don, I would like to have you briefly sketch your background, when and where you were born, where you were educated, and any previous experience you had before coming to FDA, and really what brought you in to the Food and Drug Administration.

CV: Okay, Ron, my hometown is Pella, Iowa and we retired back here about four years ago. After I retired from the Food and Drug Administration I worked for several years for the National Pork Producers Council as their Washington representative. In fact, I established the Washington office for the National Pork Producers Council. They had never had anybody in Washington until they hired me. My previous experience before Food and Drug was, of course, that I am a veterinarian. I graduated from Iowa State University in 1942, and after one year of practice was taken into the Army and served about three and one-half years in the veterinary corps of the Army. Then I spent the next seven years in two associations. And I'd gone back to the University of Illinois for graduate work when Dr. Clarkson, who was an official in the Department of Agriculture, asked me to come to Washington and begin to work in the U.S.D.A.

Then I spent eight years in the U.S.D.A. in Washington, D.C., and went out to Ames for the opening of the National Animal Disease Laboratory in 1961, and spent about six years at the National Animal Disease Laboratory, now the National Animal Disease Center at Ames, Iowa, and then came back to Washington, D.C., to Food and Drug in 1967. Dr. Clarkson, the same man who recruited me for U.S.D.A., was the first director of the Bureau of Veterinary Medicine. After about six months he was asked to become executive vice-president of the American Veterinary Medical Association. And when he took that job he recommended to Commissioner Goddard and Deputy Commissioner Rankin that they approach me for this job.

It's interesting in that respect, Ron, that instead of a big national search committee, as we now have, that they took Dr. Clarkson's recommendation. I was

at a meeting in Venezuela, and they called me and asked me if I'd come to Washington and be interviewed in regard to the job as director of the Bureau of Veterinary Medicine. So I flew to Washington, had a fairly brief interview with Goddard and Rankin, and a few days later I was called and offered the job.

RO: What year was that?

CV: Well, that was 1966, the fall of 1966. Then I began to work in the Food and Drug late in '66, and the official appointment came through about January of '67. But, it's interesting how they go through elaborate search procedures now and name a national committee to make a search. In that day and age, about all it took was a recommendation and an interview and you had a job. I suppose and I've said that's the reason they have search committees, because they did such bad jobs (Laughter) when they did it the other way.

RO: Oh, I'm not so sure.

CV: Well, I'm not either, to be honest about it. I'm not sure the new system is any better than the old system. But anyway, then I spent eleven and one-half years as director of the Bureau of Veterinary Medicine and another year approximately as Dr. Donald Kennedy's special assistant for agricultural affairs, after I resigned as director of the Bureau of Veterinary Medicine, which was a nice gesture on his part to give me a little time to get some other work lined up. I was eligible for retirement then, and I took the retirement.

RO: You resigned then from the position?

CV: Yes, I really did, but you know, to be perfectly honest about it, he was wanting to change bureau directors at the time. He changed the Bureau of Foods, and he wanted to change the Bureau of Veterinary Medicine. Don Kennedy came in as the new broom in FDA at that time. I'll never forget that he announced at one staff meeting that he'd talked to Ralph Nader and two or three of his cohorts as to who

he should be recruiting and who he should be eliminating from jobs, which wasn't very reassuring to all of us who had been working there for a number of years.

RO: Right.

CV: Did you remember that, too?

RO: No, I didn't remember that.

CV: At a staff meeting he announced that he had this meeting with Ralph Nader and a couple of others that worked with him at the time--I guess Jim Turner was one of them, and whoever else was top dog in that field at that time--about personnel. So we could pretty well see the handwriting on the wall.

RO: Who was the director of the Bureau of Foods at that time?

CV: I guess Wodicka. That's right, because I worked with Wodicka for several years, and then Miller came in after Wodicka; Sandy Miller came and replaced Wodicka. I believe that's right.

RO: You didn't come to Food and Drug until after Veterinary Medicine was a Bureau.

CV: That's right.

RO: There for a while it was a part of . . .

CV: It was a division of the Bureau of Drugs for a long time, and then, Mr. Kirk and Mr. Rankin, I guess, became convinced that it would be well to elevate it, because the activity was getting so much greater. And they elevated it, and they went after Dr. Clarkson, who had retired from U.S.D.A. by that time. He had retired from U.S.D.A. because he took the presidency of the American Veterinary Medical Association. When he got through with that job, which is really a one-year

job, they approached him because they wanted to get a really nationally and internationally known person to head up the bureau from the start. And I think Dr. Clarkson only had the job a year or so until he took the other job mentioned earlier, and that's when they asked me to take it. Bob Clarkson, M.R. Clarkson officially, had had very high positions in the U.S.D.A.

I'll never forget, he probably had been over several thousand people in U.S.D.A., and the day he talked to me about the bureau he said, "You only have 121 employees here in Washington, you can go around and pat each one of them on the head every morning if you want to." (Laughter) Quite different, the size of the organization.

RO: When you came in was there a deputy then in the bureau?

CV: Yes, I took Fred as deputy. Fred had been acting after Dr. Clarkson resigned.

RO: Fred Kingma?

CV: Fred Kingma, yes. And then I kept him as deputy. All the time I was there he was my deputy.

RO: What were some of the first things that you encountered when you took over the bureau?

CV: The first big mess was the medicated feed applications. You probably can remember when they had extensive backlogs of medicated feed applications more than ninety days and so forth. Our good friend, Al Hoeting . . . I'm sorry, I've misspoken. Fred was not acting director. Al Hoeting , H-O-E-T-I-N-G. He's now in FDA headquarters again.

RO: Yes.

CV: He was named acting director and did a remarkable job for a short period of time being a layman head of a professional organization. But he was respected. He

made a lot of good improvements in the time before I came. And he had gotten that medicated feed application thing reduced a great deal. But Roman Bounousky (Laughter) was put in charge of those things, and Roman was a brusque fellow, but he got things moving. But you remember there were details of field Food and Drug officers into the bureau trying to help reduce that backlog. It was terrible. So that was one of the first things we got straightened out, and I think Al had it pretty well under way.

The next thing I remember really, that leads into the whole residue thing, is when one of the fellows in U.S.D.A. meat inspection called me and said, "Don, we've got a couple of positive DESs--diethylstilbesterols--and, you know, that didn't shake me up too much. I hadn't been there long enough to realize the significance of that. And he did. And then they continued to get a few more. But when it hit the newspapers that they were having diethylstilbesterol residues, the concern about drug residues really heightened a great deal.

RO: What was DES used for primarily?

CV: Oh, DES. That's a good question. Dr. Wise Burroughs at Iowa Tech. University had found that using a very small amount of DES everyday in cattle feeding rations improved the feed efficiency and growth rate somewhere between 10 and 20 percent. So it really was a great boon to cattle feeders. And it was only seventy milligrams of DES a day in the feed to get this improvement in cattle growth and feed efficiency.

Now, I can't remember when the news broke about the girls having this low grade vaginal cancer who were the offspring of mothers who had taken large doses of DES to prevent miscarriages. There was a time physicians were prescribing DES in an effort to prevent miscarriages, and then it came out through large epidemiological studies that daughters of those women were having this rather rare kind of vaginal cancer. It was vaginal adenosis--I believe--and that's when the concern about DES skyrocketed. And it was ironical, because those women were given such terribly large doses every day for months, and the residues we were finding in beef were just infinitesimal. In fact the first regulatory level for DES was up to two parts per million (2 P.P.M.). They kept improving the test, and finally got

it down with radioactive isotopes, to where you could detect parts of a part per billion. When you get to that level, why you can hardly give anything to an animal that you can't find as a residue.

RO: Wasn't DES banned for a while?

CV: Oh, absolutely. But go back to the test. Earnest Umberger, whose name you remember too, was a wonderful, fine gentlemen. He had worked out a mouse uterine test which was the biological response to DES given to mice that had never been pregnant. There was no reaction in mice below two parts per million (2 P.P.M.). And with no biological response, we all figured, well, that's good enough. But that wasn't good enough when you got into radioactive isotope studies and could detect much smaller amounts. Then it was banned; after lengthy hearings and public debates, it was banned. The pellets were allowed to continue. It was given it two ways: you could put it in cattle feed constantly, or you could put small pellets in the ear, which are very slowly absorbed over a period of time. And the amount of absorption, if that was done right, was never so great that you could detect it. So the pellets were left on the market for a long time. But eventually, I think, they banned the pellets too, if I'm not mistaken. Well, I'm sure they did. When you got to where you could find parts of a part per billion, you could detect it too. So frankly, my opinion is that we overreacted to that thing, but that's very typical of a lot of these things that the media gets a hold of.

RO: Wasn't DES also used in chickens?

CV: Yes, only that's earlier. It had the same effect on chickens. It was a pellet again, implanted up around the head, and then they had what you called caponized chickens, which really meant they were the same as neutered or castrated, because the DES counteracted the male hormones. They got bigger and they were supposed to be more tender. But it was found that sometimes the pellets didn't get put in up around the head, or the head was not discarded, so they found some of the pellets; and it was the first use banned. It was not a big economic thing in chickens. Only a limited number of capons were ever raised. But the cattle, it was really a big deal.

It was a very, very big deal for the cattle feeders, and they fought it for a long, long time; but eventually it was banned. That was the first one of the drug residue problems that we encountered.

RO: Did that lead to the Swann Report?

CV: No, that's another kind of drug issue. The Swann Report dealt with the feeding of low-level antibiotics in animal feed over an extended period of time. Again, that was shown to have a beneficial effect on the growth and feed efficiency of animals that were fed: cattle, swine, chickens, and turkeys. In England they had appointed what was called the Swann Committee. In fact, they'd had a committee before; Negtherthorpe, I think was the name of the committee. Negtherthorpe.

RO: How do you spell it?

CV: N-E-G-T-H-E-R, thorpe, I think. And that committee had not found any reason to take any action, but then they appointed the Swann Committee, and Dr. Swann was a, Sir Alex Swann--he'd been knighted, carried a lot of prestige--and they decided that there had to be restrictions on the use of low-level antibiotics in animal feed. Now interestingly enough--and I don't know how many people even know this--but I had as a guest at our house a gentleman by the name of Dr. Gordon, as I remember his name, and when the Swann Committee report hit the press in England, it got reported in the *New York Times*. The headline, I'll never forget, was "Britain Bans Antibiotics." That was the little headline on the article, which wasn't true--they restricted it--but then that was the headline. And it came to my attention right away, of course. And I called Dr. Gordon--I got him off the golf course, actually, to talk to him in England--and he was just amazed there was all this excitement about this in United States. He couldn't believe it. He said, "This is just an effort on the part of our veterinary boys to get a little more control of drugs." That's the route that Britain went, that certain antibiotics to be used in feed had to be prescribed by a veterinarian. But in the United States we didn't stop at that. We decided we had to get rid of all of them. Again, the activists got a hold of the issue.

RO: Well, did they ban all antibiotics?

CV: No, that went on for years, too. The Swann Committee report was '69, if I'm not mistaken. And then the next five or six years we had study commissions (Laughter), as Food and Drug always does: one commission after the other. But I was chairperson of a fifteen-person committee who studied it for two years. The recommendation of that committee was certain restrictions on the use of penicillin, streptomycin, and some tetracyclines.

This whole issue, incidentally, revolves around the fact that low-level antibiotics causes bacteria in the gut to become drug resistant. And then there was concern that these resistant organisms, which had been shown by the Japanese to transfer their resistance to non-resistant organisms--it was done in a test tube (Watanabe was the man that had done the study)--that humans would contact these antibiotic resistant organisms in the food they ate from animals. Food from animals is never sterile, and if you have resistant organisms in animals and you make food out of that animal, you're very likely to have some bacteria on that food that can get into people. If they became infected, so to speak, with these resistant bacteria and it was transferred to other non-resistant bacteria in the human intestines, there might be a very high population of antibiotic-resistant bacteria in the intestines of people.

And the concern was, particularly for women, the possibility of transferring this drug resistant infection from the gastrointestinal tract to the urinary tract. Urinary infections in women are very difficult to treat. And that was the concern that was blown up.

Now the transfer of resistance in the test tube occurred; there was no question about it. But there was never good evidence that it really happened in animals naturally. There were several studies done by people to show it did happen. It couldn't be shown to occur naturally really. But theoretically it was possible.

RO: And this was just low-level antibiotics in . . .

CV: Yes, that's right, in feed.

RO . . . that was carried over into the tissue that we ate.

CV: Well, you know, I don't think there was concern about the meat. You bleed the animals and there weren't septicemias, so I don't think it was about the meat. It would have to be contamination, but if you've been in a slaughtering house for large animals or chickens, those are not sterile environments. You have bacteria all over the establishment. They're not sterile. They're not a hospital operating room by any standards. (Laughter) And so you have some contamination. I think they thought the contamination was on the meat from just the atmospheric conditions, environmental conditions. Opponents went so far as to say, "Well, we cook the meat. That'll take care of the bacteria." But then, it was pointed out that you prepare the meat on the cutting board and then you cut up a salad right afterwards, so you can get the contaminations in the salad that is not cooked. All of those things were raised as great big problems.

So then those hearings went on (Laughter), for years and years, too. I mean formal hearings, informal hearings, publications in the Federal Register. Actually, when Dr. Kennedy became commissioner, we had studied this matter for years. And Dr. Gerald Guest and I--Gerald Guest was at that time in charge of this whole low-level antibiotic problem as far as the bureau was concerned--and we said, "Why don't we just go ahead and do what the English did? Restrict the use to veterinarians prescription." That seemed to settle the problem in England. So that's what we proposed to do. Dr. Kennedy was happy with that. But everybody else was opposed to that. We thought the veterinarians would at least support it, but they didn't want the responsibility; they were opposed to it, too. The cattle feeders and the swine producers were opposed to it because they thought it would be costly for them to have veterinarians write prescriptions for the drugs. So that didn't get any place either.

And then it wasn't too much after that that actually I stepped out of the bureau leadership, and Dr. Crawford became bureau director. I think it's pretty much resolved, but it's still somewhat of an issue.

I have a son that's a physician, and I find that physicians are giving antibiotics over a long period of time to people now. My grandson had an ear infection when he was about three or four years old, and my son Bruce kept him on antibiotics all

winter. Rather than putting tubes in his ears, he gave him antibiotics. I understand that's a perfectly acceptable practice in the medical profession now. They used to just make fun of us for doing it in animal medicine.

RO: Is this problem we're having with antibiotics--and we'll talk about some of the other drug residues too--is it more political than scientific?

CV: It's activist-activated. Media hype.

RO: Political.

CV: Well, I . . .

RO: Well, I don't mean political in the sense . . .

CV: Well, sure and then the politicians get a hold of it. That's right. And they make hay out of it. Like Senator Kennedy got lots of mileage out of this. And who was the old boy from North Carolina, whose name slips my mind? You know, he was always having a hearing on Food and Drug. And then . . . Let's see, Kennedy, and then the little guy from California--Waxman--got into the act later on. It's great for them, they always got front page *Washington Post* publicity after hearings.

RO: You were talking about a food residue which this really is. The Bureau of Foods, now the Center for Food Safety and Nutrition (CFSAN), is involved in food additives. How did the Bureau of Veterinary Medicine and the Bureau of Foods resolve the jurisdictional issue?

CV: It's very interesting that you asked that, because before I was director of the bureau and before Dr. Clarkson was even director of the bureau, drugs that were going to be given to animals had to be treated as animal drugs and as food additives. Do you understand the language?

RO: Yes.

CV: So they had to get clearance of two bureaus. And those drug companies were just about driven up the wall trying to get clearance in Bureau of Foods for food additives. So they revised the Food and Drug Act to include an animal drug section to get around this. So they are combined now; but there had to be consideration given to the food additive aspects. It wasn't necessary to have a food additive application approved and an animal drug application approved--just one. But we had to confer and . . . yes, and really take the advice and recommendations of the Bureau of Foods in regard to the residue aspect of the food from the animals that were given the drugs. That came along with the animal drug amendments, which were enacted just before I got there, 1966 or '67. And really it didn't simplify things as much as you would think. We still had many controversies and struggles between the two bureaus. But the responsibility for the safety of food from animals is given drugs directly or in animal feed was entirely with the Bureau of Foods. We had to follow their advice and recommendations.

RO: In addition to the antibiotics, there have been other drug residue problems.

CV: Yes, I think the first one of those that I remember was the nitrofurans, the whole group of nitrofurans. You know, there are certain things that stick out in your mind. I remember seeing a memorandum from one of the veterinarians working for Bureau of Foods--and I don't know why they hired veterinarians to do that over there, because they weren't food scientists--saying that one of the nitrofurans was a carcinogen. Well, that put it in a very special category because of the DES proviso in regard to carcinogens.

So I took it up with Mr. Kirk--that's back when Mr. Kirk was there--and I said, you know, "I just don't take this lightly. When somebody over there tells me that we've got a carcinogen, I've got to do something." Well, his advice was, "Don't get too excited," (Laughter) and asked me to refer it to some experts. And I had two go-arounds with the experts and they couldn't conclude that it was. Frankly, the Bureau of Foods people had never even looked at the pathological slides, and so a very well known pathologist--Dr. Eppley of the Eppley Cancer Institute in Omaha, I

believe--he examined the slides, and based on his examination of the slides, he couldn't say whether it was or wasn't. I mean there was some question about it.

So really this is still dragging on, I believe. The nitrofurans, I believe are still an issue. I think Food and Drug finally published a year or two ago an intention to withdraw approvals, some of them, and I don't believe it's been acted on finally. So this is what--from '69, twenty-one, twenty-two years?--I think it's still going on. Dr. Guest could tell you in a minute where those things stand. Dr. Guest then became director of the Center for Veterinary Medicine, as it is now called, after Dr. Crawford.

(Interruption)

CV: Chloramphenical is another one. It's a very effective antibiotic that had been shown in people to have a marked adverse effect in about one out of thirty thousand people, as I remember the figures, it caused an irreversible anemia. And it was fatal. A little bit like AIDS; if you had it, you didn't stop it. And so that led to its being greatly restricted for use in human medicine. It was never banned, but it was always . . . you know, it was recommended as a drug of last resort. Well, it was useful in animals too--very effective drug in animals--and very widely used. But then the concern came about whether or not there were residues of chloramphenical in the food of animals. I can't remember the exact levels, but there was some that you could detect. So that lead to the banning of the use of chloramphenical in food-producing animals. It's still available for use in dogs and horses, I believe. And there has been all kinds of trouble with that, too. I'll bet you remember that there was a chloramphenical for use in aquariums. (Laughter) And the veterinarians would get that drug and make it up into treatment for other animals.

Interestingly enough, Ron, I got involved in a lawsuit in regard to chloramphenical on a human death after I retired out here in Pella. A cattle producer out in Kansas had lots of problems with a herd of feeding cattle, and the veterinarian finally prescribed chloramphenical and told him what he was doing and warned him. And this fellow was a little careless and he had some cuts on his hands, and he absorbed enough chloramphenical that he died. His son-in-law was a dentist, and his son-in-law started looking into it, and they sued the drug company. And I was

involved as an expert witness as to what was FDA's role, which was all I did. But they finally settled it out of court, but that's the way those things do happen, and it could happen, of course. I think there was not much question but what he developed this anemia as a result of this exposure to chloramphenical from treating his own animals.

RO: There was a new animal drug approval process that your bureau was responsible for. When a company would submit an application for the approval of these drugs, did they have to prove that there was no carry-over into the tissue of food-producing animals?

CV: Yes, what we called them was the NADAs: New Animal Drug Applications. And they had to submit evidence of the drug's effectiveness, just as for human drugs, but if it was going to be used in food-producing animals, they had to give us evidence that there were no residues or that if you would wait so many days after administering the drug--we called it withdrawal period--that there would be no residues or at least it would be down to a certain level. There were elaborate studies done in laboratory animals to try to determine what was the no-effect level for the different drugs. Actually, that was pretty much the Bureau of Foods jurisdiction, and the Johnson Memorandum which you had on your list was all about this. What we got involved in was not only the residues but the sensitivity--how low a level could you detect residues in the tissues or the milk or eggs, for that matter. And there was a time when two parts per million was considered good at the time of DES approval.

RO: Yes.

CV: But then the time came when that wasn't nearly good enough and we got into parts per billion with the different analytical methods. And it was always interesting to me how much controversy there was about the reliability of the different analytical methods. You could get just about as many opinions as there were analysts on those methods. There was this elaborate system of sending it to the AFDC, wasn't

it? Who ran that matter of certifying the accuracy of analytical methods? They had elaborate procedures. They . . .

RO: It was the A.O.A.C.

CV: Yes, the Association of Official Analytical Chemists. They had that elaborate method, but again it took several years to validate a method. You'd submit it and they'd refer it to referees and they'd all run test and get reports back and then they'd debate it. But the drug companies couldn't wait three or four or five years for one of those to be validate. So people would have to make decisions as to whether it was good enough, and that was done again by the Bureau of Foods. We'd take their recommendations and that led to controversy between the two bureaus. We thought in many cases they were super conservative or that they wanted too much. But they had the idea that if you were dealing with the health of people and consumer food safety, you couldn't be too careful.

RO: You mentioned that Johnson Memorandum, and that had to do with one of the . . .

CV: Analytical methods for drug residue.

RO: That was a list, really, of the drugs for which he felt there were not suitable analytical methods or . . .

CV: Actually, it's interesting the way things develop. Dr. Johnson was director of one of our divisions, and he had some chemists in his division. So I said, "Ken, would you work up a list of the drugs that you folks consider highest priority for meat inspection to be analyzing for?" Because we wanted to give U.S.D.A. a list of priority drugs. They couldn't test every animal for everything. Fred Kingma used to say that if you tested every animal for every drug you'd have to import the ones to eat, because they'd all be used up in the testing process; and that's about right. So it was an assignment to come up with what was the highest priority drugs for meat inspection to be testing for.

RO: Now, meat inspection, that was U.S.D.A.?

CV: Yes, that's right. You see they had that responsibility of inspecting the animals that were slaughtered, and then they incorporated in their program a testing program for drug residues. That's another interesting point. They took routinely three hundred samples--random selection, all over the country--and they used that not as an indication of how much residue they'd found in those particular samples, but as a survey of the nation. Three hundred seems like a small number, but if you go to the statisticians and you start talking to them about the numbers of chickens, turkeys, cattle, and swine, the population is so huge, that it doesn't do much good to . . . a thousand is not much better than three hundred if they're selected correctly. They calculated that three hundred gave them an accuracy within 5 percent. You could go as high as three thousand and maybe you'd raise it up to 4 percent. It's a pretty detailed procedure to test all these things analytically, so there was a limit to what they could do.

But in trying to help them concentrate on what would be the most likely to be a problem, we decided to give them a list of drugs that we thought they should concentrate on.

Well, Dr. Johnson and his chemists took that assignment, and they came up with a list of at least twenty-seven drugs for which they said there were not adequate analytical methods. That started a big hullabaloo. I've often thought back and wished I had just sent it over to Dr. Wodicka and said, "Dr. Wodicka, you've got a problem." Because it was his problem. They'd approved them. But I tried to defend them from the standpoint that I didn't, first of all, think the residues were all that serious, and secondly, that if we had to take all those drugs off the market, it would really seriously interfere with animal disease treatment.

I didn't handle that very wisely, as I look back. I tried to get some of the differences worked out within our bureau in regards to analytical methods, but eventually that led to the big hearing that Senator Kennedy held. I don't know what year that was, but . . .

RO: That was about '75, wasn't it, '74, '75?

CV: Probably about that time. He sent an investigator into the bureau, who spent thirty days talking to everybody that was dissatisfied that he could talk to, and he was a very good interrogator. You'd make some little slip about something and he'd dig and dig and dig, and finally he'd have them produce the memo they were talking about. So I think there were finally nine staff members that were subpoenaed to come before Senator Kennedy for a hearing. And there was a litany of all the terrible things that I had done to defend the drug industry at the sacrifice of the consumers of the country. That led to several reviews of that whole issue. And as I mentioned earlier when we were talking before the interview, there is a rather large book that is a report of the last one of those investigations by a group of outsiders. They concluded that I really had never done anything criminally wrong. And I was tempted to spend some money to see if I should pursue that, because I didn't think there was any question of criminality.

And there's quite a long list of drugs that they looked into and, you know, I'm happy to say that over the years, most of those have been vindicated. The decisions we had made have been vindicated. There was a mastitis treatment--that's a disease in dairy cattle, milking dairy cattle--and a high dosage of penicillin and streptomycin that was being severely questioned. Turned out to be routine procedure now over the years; it's just used all the time and considered to be one of the very best tools they have against the disease.

And Mercadox was a swine drug, and it was under all kinds of questions, and it's still being advertised very widely in the swine magazines that I see. The nitrofurans were in that whole issue, too. I don't know what all the rest were. Oh, there were eight or nine different drugs that were controversial.

RO: That was '75, or the seventies somewhere along in there. Were you in FDA when there was a problem with polybrominated biphenyls, PBB?

CV: Yes, that was drug residues, too, in a way.

RO: Yes, it did end up to be drug residues.

CV: Yes, it surely was. That was a case of where some fire retardant material known as polybrominated biphenyls was mixed by mistake in some dairy cattle feed and distributed by the Michigan Farm Bureau feed companies. At very high doses it was rather toxic. And so it caused a heck of a problem in those first herds, but the farther away from the primary exposure you got, the less the effects were. But that led to a lot of controversy in Michigan. In fact, the Michigan food stores were advertising at one time "No Michigan beef," because the consumers were concerned about it.

Our principle participation was to appoint a task force of scientists to go to Michigan and make a detailed epidemiological study. We did that, and you know, other than those primary exposures, there was no indication that the lower levels had done any harm to the animals.

Frankly, I can't remember the level of the residue problem with that and what the levels of analytical capability were, but it was another example of the media getting involved and hyper-reacting.

RO: Weren't a lot of the herds destroyed?

CV: There were some. There was a Michigan developed program of indemnity to pay the owners for herds destroyed. There was one farmer that even shot his own animals. They weren't very good animals and they weren't producing very well, and he decided that it was a result of PBB poisoning, so he shot them and tried to collect. There was a series of hearings held by one of the senators in Michigan. I won't mention his name, because I'm not absolutely sure. But they had a series of hearings around the state, and he just encouraged farmers to come up to tell their horror stories, you know, about all their experiences. Every time one would report his problems, as soon as he sat down there would be some lawyer rush to the front and try to talk to him about a lawsuit. And that senator never let the scientists report on their findings until the fourth hearing, which was at the capitol in Lansing, and then he gave them very little time. He apparently didn't really care about the facts, either. It was political, as you say. all the way. That's an example.

There were a couple of other feed-poisoning mix-ups that were pretty serious. PCBs, that's the polychlorinated biphenyls, was't it?

RO: Yes.

CV: And it's used to heat transfer. And I remember there were some leaks in the . . .

RO: Heat exchangers.

CV: They had these big heat exchangers that they heated fish meal in. They had some leaks, and then the contaminated fish meal got into the chicken feed. It caused a real serious problem as far as the chicken industry was concerned. Holly Farms was one of those that really had a very serious loss.

There is one thing I forgot in regard to the DES the diethylstilbesterol. When this became a problem in the early fifties, Congress enacted a change to the Food and Drug Act which said that an animal drug could be used even if there were residues if there was no residue above a certain level. They established a level at the sensitivity method at that time, which was Umberger's two parts per million. So that's why DES was continued in use, because there was no evidence from the tests in the sensitivity of that time that there were any residues if the fourty-eight hour withdrawal period was observed. Then the methods became more sensitive, and that was not good enough any more. We did take the feed use off the market before the pellets, because there was a long time before the analytical sensitivity was adequate to pick up residues from implanted pellets, because they produced such a slow release that one had to get down to the radioactive isotope studies--which were really down in the parts of a part per billion--to be able to detect them. Once that was discovered, the activists succeeded in stopping the ear pellet use.

But there's a whole section in the Food and Drug Act that's called the DES Proviso. I saw that on your list. And I can't quote it anymore but this is basically what it was: that it is legal to use a drug in animals even if it is a carcinogen if there are no detectable residues of that drug in the food. At the time they passed the DES Proviso it was two parts per million for DES, Umberger's Test. I used Umberger a lot for a consultant after he retired. Excellent man, his test was used in virgin mice. If it didn't get a uterine response in virgin mice, how much more sensi-

tive can you want? What does the chemistry mean if you don't get any biological response? But that wasn't good enough for the activists.

You mentioned salmonella while we had a break. That's been an interesting program over the years. I think they're trying to crank it up again in the Food Safety and Inspection Service. Salmonella are responsible for most of the food poisonings in people, and animals have salmonella in their guts; there's no question about that.

RO: I remember several years ago G.A.O. did a study in Food and Drug where they found that there's a high incidence of salmonella on edible chicken meat.

CV: This goes back to what I was saying: when you take a live animal into a building, and you convert it into food, that's not a nice business. And you get that environment contaminated--and you can't do it any other way--you're going to have some of those bugs that those animals have in their guts or they carry on their skin or their feathers get in the food. It's almost impossible to do otherwise.

Now, the chicken processors, last I heard, were still putting chickens through a chlorine rinse, and that took off almost all the surface bacteria that . . . Of course, the safety of the chlorine rinse has been challenged over the years too; but I guess with the use of chlorine toothpaste for teeth, it's pretty well resolved there's no particular danger about that. But that was the case of the salmonella. I'm not sure you can kill live animals at one end of a building and process them all the way through and not have food at the other end with some environmental contamination. The chickens are about the worst, because you put them through one of these scalding tanks to loosen the feathers, and you push out a little feces in the process, and that whole tank gets contaminated, and they continue to go through it. I don't know if your parents used to do it on the farm, but then you put them in the bucket one by one. I guess if you threw the water away between chickens maybe you could avoid that problem, but you don't do six thousand chickens an hour with that kind of a procedure.

commerce and therefore subject to federal government jurisdiction--FDA and USDA.

RO: Was that ever challenged?

CV: I don't think it ever was. I think it's a logical conclusion. But that had a lot of bearing on drug residues. Because we could consider animals starting to move from a farm to federal inspection as food and therefore any contamination that occurred was illegal residue or illegal contamination of food under federal jurisdiction.

Now another thing that has always interested me about this whole enforcement is that when FDA approves a food additive application for human food, I don't know if any enforcement is ever carried out to see whether the firms are living up to the requirement of that application: how it's used; what the conditions are under which it's used. Isn't that true?

RO: I don't know.

CV: Here you're approving a direct application to human food, and there is no particular follow-up. And here we got all excited because animals once removed from human food were given something that might come through in the food from the animals. I know Dr. Wodicka said one time when we were having about 2 percent violations of DES, he said, "I wish I knew if any other food additive application we approved was that well enforced." And that's always been interesting, because the inspection of the food establishments of this country, as you and I both know, is not very thorough. They get around to inspect them about once in ten years or something like that?

RO: Well, some of them more often, but it's a good interval. Of course we are trying to inspect those that would present a real health hazard more frequently. You mentioned, while we were breaking, about the nitrates and the problems that we had.

CV: Yes, that's another interesting story. That didn't take quite so long to resolve. M.I.T. did a rather extensive study of nitrates in mice, and it was a very good study. They recommended on the basis of that study that nitrates should be given some more very careful consideration because there was some indication they caused tumors. Dr. Kennedy and the assistant secretary of Agriculture at that time, Carol Forman, decided they were going to ban nitrates. And frankly, a young pathologist in the Food and Drug Administration, the Bureau of Foods, was the one who had made the determination that yes, there was evidence that they were carcinogenic. They handled it in pretty much of a hush-hush manner until they proposed actually to withdraw the use of nitrates. This is a product used for curing hams and bacon and corn beef, also put it in some of the sausages. It had tremendous economic importance. I remember the president of the American Meat Institute told me at one time that the economic significance of nitrates was equal to women's wear retail sales, furniture retail sales, and the booze industry. That was the extent. Not each one, but combined.

Well, the meat industry and the pork producers particularly really opposed this very strongly. The final outcome was that Al Kolby headed a final review, and they concluded there was no evidence that nitrates were carcinogenic. That was only about three or four years later. Carol Forman came before a congressional committee and said, "Yes, we made a mistake."

RO: Well wasn't that because the nitrates when heated form nitrosamines? Is that . . .

CV: Well, that's another part. The nitrates in the stomach are converted to the nitrosamines which were considered to be carcinogenic--not nitrates per se, but the nitrosamine. But the final conclusion was that there was no basis for concern, and so they're used today. But it did have tremendous economic effect on the pork industry for several years. Bacon just about became a bad word for a while, you know, and it was so popular before.

But that's one of the few times that I ever knew a government official to admit they made a mistake.

RO: Yes, it's seldom.

CV: (Laughter) And Carol Forman did it at that time.

(Interruption)

CV: One other residue that has gotten a great deal of attention over the years, primarily in turkeys and swine, is the sulfonamides, and the particular drug in that group is sulfamethazine. It was approved with a withdrawal period, as I recall. And the turkey people were the first ones to have a pretty high level of violations. We had some meetings with them, and they corrected it very quickly. I mean they got it down to less than 1 percent on the basis of meat inspection sampling.

The swine people use it. There was a very popular feed additive called ASP-250. And that's aureomycin--which is another name for tetracycline, or their trade name--and sulfonamide--that's sulfamethazine--and penicillin used in combination as feed additive in swine. As we discussed earlier, there is some question about some of these lower levels--and this is not really a low level--whether they have a disease-controlling effect as well as a growth-promoting effect. This one is probably one that is the disease-preventing effect.

The swine industry was using it very widely, and then the residues detected by meat inspection climbed as high as 13 to 14 percent of the samples taken at one point. We really were very rough on the swine growers. And they launched an industry-wide program with a lot of help from U.S.D.A. and the feed mills, and they got the positive samples down, to 4 percent, I believe. And so everybody said, "Well that's pretty good," and kind of relaxed, and then the positives came back up again. Now it's very low again from what I read.

But now the controversy is whether sulfamethazine is a carcinogen or not. And that laboratory out at Pine Bluff, Arkansas, has been studying this for four or five years, and their reports are about to come out. It's always about to come out. If they have concluded, in fact, that it is a primary carcinogen, then I guess Food and Drug will have to reduce the level of sensitivity or withdraw it from the market. Currently the level of sensitivity is one-tenth of a part per million, I think, and that's the tolerance, but if it is found to be a carcinogen, the tolerance will go lower.

Now for the benefit of anybody ever reading this, I think that sulfamethazine is not a primary carcinogen. And I think there has been lots of evidence to show it isn't. The studies that have been referred to were some studies done I think in monkeys where they did develop hyperplasia of the thyroid. And then there was evidence of hyperplasia in the lungs. But when the drug was withdrawn, the lesions reduced, or reverted. Now carcinogens don't do that. Cancer doesn't get better by itself. And we had some very good scientists that pointed to that, but FDA always seemed to brush this off. They don't want to hear it. And there was some reports that the Pine Bluff laboratory was going to come to the same conclusion. Dr. Guest is still talking real tough about sulfamethazine, so I don't know what's been happening.

Again, people are treated with this drug. (Laughter) It's almost funny. If you go to a physician and he decides you need a sulfonamide, he'll start you at eight grams a day, and then he'll go down to about four grams a day for ten days. You couldn't get that much sulfamethazine from eating pork if you ate, you know, tons.

RO: We've kind of skirted the real issue. We've talked about whether or not these compounds are carcinogens; but don't we really need to talk about the Delaney Amendment?

CV: Yes.

RO: Do you really think that the Delaney Amendment as it stands now is something that is practical from a scientific standpoint?

CV: You have to have a better definition of what's a no-effect level of carcinogen to make it practical. If, as I said, in DES going down to parts of a part per billion and ignoring what the biological significance is, it is not a sensible use of it.

That reminds me that after one of those first DES roundups, Dr. Lehman, Dr. Dick Lehman, who was a Ph.D. scientist in the bureau and a very good one, said, "You know, we had such a fiasco in this DES case the first time around, we've got to have something better." And so he proposed a way to get at no-effect level. Mr. . . . Who was the deputy that's been acting so often? Gardner.

RO: Sherwin Gardner.

CV: Remember he went before a congressional hearing and he talked about defining zero? And Mr. Whitten had a lot of fun with him for years about the man who can define zero. But that's what he was talking about. Some definition of what is no effect. If you could get that, get an agreement on it, then Delaney Amendment is good. But until you get that, why as long as you just continue to hunt for less and less with more and more sensitive methods, I don't think it has any practicality. But it will never be a practical solution in my opinion. Any time we have a hearing on it, the activists get up and say, "Well, are you in favor of cancer?"

RO: Sure.

CV: And no congressman is going to ever go on record in favoring cancer.

RO: A scientist mentioned to me one time that we were going start into looking for nothing and everything.

CV: Yes. I remember that when I was working for the pork producers after I retired from FDA, there were three or four days of hearings on the food additive amendments. Oh, boy, we thought we did so well. But then you get about three or four of those people that are fairly articulate, and they start talking about, "Well, we don't know what the no-effect level is, do we?" "No, you don't really." "So it could be a factor in causing cancer." "Yes, you have to admit it could be." And that's where it ends up every time.

RO: We can come back to this, but there were a couple of other things I'd like to touch on. You, I think, were responsible for assigning some of your headquarters veterinarians to the field and there . . .

CV: Actually I don't deserve credit for . . .

RO: You don't deserve credit for that?

CV: That was Dr. Goddard's idea. That was in effect when I got there.

RO: Oh, and I always thought that you were responsible for that program.

CV: I may have helped select one or two, but then the decision to have regional veterinarians, as we called them, was Goddard's decision.

RO: I see.

CV: You know, he had the policy of moving more actions to the field?

RO: Yes.

CV: I think he thought there were some of the decisions that were "bottle-necking" in the bureau that could be made in the field if we had regional veterinarians. It never quite worked out though.

RO: I don't think that there are any of those positions left in the field.

CV: None left now?

RO: I don't think so. Probably Ed Sterner was the last one in Denver, and I think he retired within the last few years.

CV: And those were some good men. Were you ever in the district where you had one?

RO: Sure, I helped indoctrinate Dr. Levy.

CV: Okay, in Baltimore.

RO: I think some of the problem was that it was never clearly defined exactly what they were supposed to do.

CV: They had no authority, did they?

RO: No. You know, a few of the veterinarians in some of the field offices did a lot of reviewing of the veterinary drug issues that came up, which was good. But some of the others didn't seem to have much interest in doing that. I know some of them were very successful in developing a better federal-state relations program than some of the others.

CV: The man out in California was good at that, I think. What was his name again? Former meat inspection man.

Actually, you know it was a matter of . . . they weren't selected with a particular expertise. If they wanted them to be reviewers of drug problems, they should have gone to people who had special knowledge in animal drugs. But they didn't; they just took veterinarians. Some of them were ex-practitioners. You know, it never worked out. We tried real hard working with your district directors to make a program for them.

Now McMillan in Atlanta felt they got a lot of good out of his regional veterinarian.

RO: Well, I think it depended a lot on the veterinarian and a lot on the district management how well that program worked. I mentioned Dr. Levy. When he finally was transferred from Baltimore to Philadelphia, they used him a lot in federal-state programs, and they really thought that he developed successful programs.

CV: He was certainly a willing worker, wasn't he?

RO: Oh yes. Here I thought all along that you were the one that was responsible for that program. You and Paul Hile.

CV: No, you can't blame us. Goddard did that. I think maybe Fred and I helped select the last one or two, but the decision was made before I got there. And the changes in the law for the animal drug act changes were made, too, before I got there. Just before I got there. There's something on your list that leads me into that.

Oh, the extra label use. That is so interesting. Section 502 of the Food and Drug Act, which deals with human drugs, says, "A drug or device shall be deemed to be misbranded if its labeling is false or misleading in any particular, if in the package form unless it bears a label containing . . ." and it goes on. Now we go to 512, which is the animal drug part of the act. And it says, "A new animal drug shall, in respect to any particular use or intended use of that drug, be deemed unsafe for sections of 501 and section 402." That's the human drug and the food additive application and unless there is in effect an approval for the use. Well, now this "respect to any particular use or intended use of the drug" is different than the one in human drugs, if you recall, because it didn't make any mention of the use. So that section was changed to get around the dual approval of food additive applications and drug approvals. And they put this "use or intended use"; they agreed to that at those hearings to get around that double clearance. Well, we knew for years and years that veterinarians were using drugs a little differently than they were labeled. They'd be quite different in some cases. Larger doses, sometimes they were approved in only one species. Let's say they were approved for use in chickens: they would use them in turkeys even though turkeys weren't mentioned on the label.

Well then I think it was 1983. Dr. Crawford decided--he was director of the bureau at that time--that this misuse of animal drugs was so severe, they had to give a strict literal interpretation to this use or intended use, which said that a veterinarian could use the drug only as it was labeled. If it said you had to give three thousand units per pound body weight, you couldn't give more. Even though practice might have shown over the years that the resistance of that drug had developed and you needed to use three time that much. Or you couldn't use it in turkeys, as I mentioned, unless turkeys were mentioned. And this caused a real to-do, because there wasn't hardly any practicing veterinarian in the country that wasn't using some drug in a manner other than strictly according to labeled use.

Now if you remember the approval process, a drug manufacturer is not going to come in every time they want to change the dose or add a species, because they would open up the whole approval process. Some of the decisions that were made fifteen years ago or ten years ago when standards may not have been quite as high would all be subject to review, so they just didn't bother to change those labels.

And so the veterinarians, the practicing veterinarians, were caught in a real bind. They were using drugs . . . If they used them according to labeled use they knew they weren't going to be effective. And there were some species in which they knew they were effective, but they weren't allowed to use them if they followed the labeled directions. So this led to a real big controversy, and it's finally been resolved by compromise on both sides. The veterinarians now are not supposed to use them other than in accord with labeled directions unless they have explored all other possibilities, and then they have to discuss it with the owner and tell them what they are doing and all of the possible complications. I think it isn't completely resolved yet.

RO: Well, if they were so effective for a species that they hadn't been tried on, why wouldn't the sponsor of those drugs test them on the new species?

CV: They could, but they'd have to go through the whole series of test. Lot of expense, you know. And some of those are fairly old drugs. There might even have been some that were under the old, I mean, the generic provisions. Now don't ask me about the generic approval, because that's after my time. But I think there were some of those that were far enough back that there were generics, so there was no particular sponsor any more. Everybody was making them. Who was going to step out and do the work for all the rest of them? As long as there is a new drug application on file, and you don't have generic use, then if somebody does the work, it applies only to his application, unless he includes other people and gives them license. But once it has been generally approved, like the antibiotics in general have all been, there's no point in John Companos, for example, doing the work, because everybody else will piggyback on it and he can't stop them. So it was a real dilemma. And it was the interpretation of that section of the act, which I think is correct legally, that led into this whole extra label controversy.

RO: We know there have been some problems with a lot of these veterinary drug houses selling prescription veterinary drugs to just about anybody.

CV: Yes, there is no question there have been violations in that regard, and veterinarians selling prescription drugs out of their offices to customers. FDA has tightened up the enforcement a great deal and they've made some good legal cases. Veterinarians are much more sensitive to the illegalities, I think. But, I'm not sure it's still as good as it should be. Again, for the benefit of some people that read this, they might say, "Well, why could it be controlled in human medicine and not animal medicine?" When you go to a physician, he writes out a prescription, and you go to the drug store and you buy the drug. When treating a herd of two hundred cattle, or maybe five hundred hogs, you don't go to the drug store to buy those drugs. You've got to get those drugs in large packages. A veterinarian just about has to have them on hand in his own office. So the control there is more difficult.

And this leads to the medicated feed problem., too. It's different in medicated feed. There are prescription drugs for use that get into medicated feeds without a prescription. And when you go to one of these big feed mills and you see them dumping drugs in the feed mill, you know, in fifty pound quantities, that's so different than human prescription of drugs and drug uses that you can see there is certain to be lots of problems.

RO: That leads us into the good manufacturing practices (GMPs).

CV: Yes, GMPs for medicated feeds. As I recall this, and I think I am right, Jim Gessling wrote the GMPs that were in effect for about twenty-five years one night at home. Mr. Kirk said, "Jim we've got to have them tomorrow." So Jim sat down that night and worked all evening in the kitchen and what he came up with the next day became the GMPs. That's about how much consideration was ever given to the practicality of those GMPs in the outset. Nobody thought they were going to be enforced too completely, but they were on the books. Then this whole residue concern comes along and they get concerned about what and whether they are doing what the regulations require and if they are causing cross-contamination.

That proved to be a big problem in sulfonamides, incidentally. You could hardly use a feed-mixing equipment to mix fairly high levels of that ASP-250 and not have subsequent batches coming through with fairly high levels of the drug again. So if you mix for the pigs that are supposed to get the ASP-250, but then you've got fattening hogs that don't need it, and they're going to go to market. The feed you mix for them that went through the same equipment is going to have enough to cause some residues in those hogs that go directly to market. Originally there was not too much care given to this in feed mills. Farmer mixing was even worse for that kind of a problem. But when those things became evident, then good manufacturing practices at feed mills became much more important. When the inspectors started to inspect them carefully, they found lots of problems, as you would expect.

A feed mill, again, is not a pharmaceutical firm, you know. It's entirely different. You've got dust, and material is there in bags, and quantities. I doubt whether we can ever handle animal drugs with our current animal production methods in small quantities. Treating one animal at a time, that isn't done much anymore.

I have so many remembrances, but I . . . One of these antibiotic review committees, which was appointed by Dr. Kennedy, I guess, had a cattleman on it from Colorado, a big cattle feeder. We had a couple of activists on it, too, because you had to have a balance, you know. They didn't know "beans" about it, and Mr.--I'll think of his name pretty soon--talking about feeding his cattle; I think these activists thought they went around with a five-gallon bucket and gave each one a scoopful everyday. And Mr. started talking about how many tons of feed he mixed everyday for his cattle, and this fellow was just aghast. And to his credit, he just didn't talk very much anymore, because he realized that it was entirely a different problem than he thought it was.

Interestingly enough, Canada banned DES before we did for use in animal feed. And it wasn't long until they were real concerned about not being able to get the right kind of cattle for their restaurants and hotels in Canada. They came down with a big entourage of people headed by their minister of agriculture to work out some kind of a certification program so these cattle that got DES in feed could get into Canada. That's when there was a certification program for a while; feeders

would certify that the cattle had been off DES feed for a certain number of days or never had it in the feed.

RO: You mentioned a while back about the congressional investigation there was back in '75 or so about your management practices or management style in the bureau. You were kind of accused, I guess, of being soft on industry, not a very tough regulator as far as the FDA was concerned.

CV: That was the opinion that some people had--no question about that. And, you know, Peter Hutt was always a pretty fair fellow, really. He recognized that what we were trying to do was draw some balance between economic advantages in drug use and this matter of consumer protection. And some people would argue that the Food and Drug Act doesn't allow for any economic considerations.

RO: Yes.

CV: And I couldn't ever accept that as far as animal drugs was concerned, and so that led to a lot of the problem.

I mentioned that "dry" cow treatment in large doses as a mastitis product. They gave it an extensive test in New York state under the DHIA program, and production in those herds was just sizably better than it was if you didn't use it. Still we had people trying to keep it from being approved for all kinds of imaginary problems. It's been used now for years and considered to be a mainstay in mastitis treatment, and none of those terrible problems that were going to result ever developed insofar as I know.

Another thing you know--it's true for all of Food and Drug applications--it's less controversial to say no than to say yes. You're very seldom accused of anything bad if you say no.

RO: Gentian Violet. We didn't talk about Gentian Violet.

CV: That's another interesting one, as old as there are medicines. It was used and used and used for direct skin applications and many other things. And still when it

was used in animal feed then there were some that wanted it to be declared carcinogenic. Then the issue was whether it really was a food additive. It had been used for so long. The food additive amendments were adopted when--1958?

RO: Yes.

CV: And Gentian Violet was used before that, so then it was argued that it was safe under the grandfather clause.

RO: Then you recognized the mistake.

CV: Yes, and all that got to be a big to-do about whether it was a gras substance or whether it was in fact a food additive. I don't know where it stands now. Do you?

RO: I don't know, I just happened to think about it.

CV: Again considered to be a pretty important drug in certain chicken flocks to keep down the mold and yeast infections in chickens.

RO: I remember when I was a kid, we used to put it in the chicken water.

CV: Yes, and I bet you used to paint wounds on animals with Gentian Violet, you know.

The federal-state cooperative programs you have on your list. I always thought there was a wonderful opportunity for federal-state cooperation in all of the programs. I don't know if your experiences would bear this out, but it seemed to me that it depended a lot on the district veterinarian how active it was.

RO: Remember we had an educational program for a long time and we put on workshops for a lot of the states on how to make medicated feed inspections. I was just wondering what your view was of the program and if you felt from the bureau's standpoint if they were effective?

CV: You know, the main problem that I always heard with the state reports were that they were not those long narrative reports like your Food and Drug inspectors made. I always wondered why Food and Drug hung onto to those narrative type reports for so long. Are they still doing it?

RO: Well, there are some inspections that lend itself to a checklist approach, but the main objection to a checklist was that it could channel the inspectors to look at those things only rather than looking at the entire operation.

CV: Of course, that's what we tried to accomplish in GMPs for medicated feed. A checklist finally of the things that were critical.

RO: They're used a lot now.

CV: . . . which has reduced the time a great deal.

RO: Oh sure.

CV: It seemed to me it's a natural to have coverage, but we all know that state employees are probably more political than federal inspectors.

(Interruption)

CV: I guess we talked a little bit about this DES proviso, and you asked me whether the Delaney Clause was a possibility. This got to be known as Sensitivity of the Method, S.O.M. And as I told you Dr. Lehman was the one who first said, "We've got to have something better than we had before." But he also introduced the idea of metabolites, which had really never been carefully considered at Food and Drug, and it was so scientifically correct. Nothing you ingest--I shouldn't say that--but anything that's biologically active that you ingest, is going to be metabolized. So what do you look for if you're looking for residue? The metabolites are going to be different in twenty-four hours, forty-eight hours, seventy-two hours, maybe ten days. There's a constant change taking place. So an analytical method

for the intact drug, taken two or three days after the drug was ingested, may be not be worth anything.

(Interruption)

Well, on my birthday which is July 19, way back, we published a fairly simple sensitivity of the method document, but frankly the scientists began to pursue this, and they worried about minor metabolites and "bound" metabolites and everything else, and it became unworkable. And I don't think there is any resolution yet. But it always seemed to me it was so simple: if you're going to make an analytical method for a drug, and you decide in advance that five days was an adequate withdrawal period, or that it was a practical withdrawal period, then you studied the metabolites that were there at five days. We learned that those metabolites are many and many, and there are major ones and minor ones, and you just have to make a decision as to which major ones you are going to look for, because you can't find them all. You can't have a method for all of them or you may have as many as fifteen or twenty tests for one substance if you look for all the metabolites. So unfortunately, I don't think the thing had ever gotten anywhere, but it's a very sound principle.

RO: Well, you'd have to do those studies in vivo.

CV: Oh, of course. Yes.

RO: Could it vary from species to species?

CV: Possibly. Possibly it could. Yes, I think it's a good chance there would be, because the way the rumen metabolizes would be different from the way the single-stomached animals would metabolize them. I think that's true.

So it's not simple, but it's the only way to be sound, because there is no point in looking for the intact drug a week after the animal has been given it. It's not going to be there. And that's why a lot of the analytical methods that went way back were okay, because they couldn't find it for that particular substance.

In a way that argues for Umberger's biological methods, you know. Why not look for what's the biological effect, instead of all the chemical analyses?

RO: Of course that's what they found, too, in pesticide residue analyses, that if you spray on a pesticide, you might not find the parent compound, but the metabolites from weathering were a problem.

CV: And you know if we could just agree on some biologically significant measurement. You know, the worst example of this, Ron, that I think I've seen now is in regard to aflatoxin. A year or so ago after we had some dry weather they made some people in Iowa discard their milk, because they were finding a *half a part per billion* of aflatoxin in the milk. *Half a part per billion*. And you really need a pretty high level of aflatoxin in peanuts, going back to the African studies, to have a carcinogenic effect. And I figured out once that a part per billion is one second in thirty-five and one-half years. So here we were making them throw milk away because they had the equivalent of one second in seventy years. What does that really amount to?

RO: Well, that is the reason that the Delaney Amendment as it is right now is probably not practical. On another topic, you worked for several different commissioners, and I would like your impressions of those you worked for.

CV: Well, you know I'd rather not "seal" all of this recording. I'd rather have it be of some use. I always thought that Dr. Edwards was an excellent commissioner. Dr. Kennedy's philosophy was entirely different than mine; he was very much of a liberal, and I was more of a conservative. I always respected Mr. Rankin when he worked as the deputy commissioner. Let's see, Dr. Schmidt. I worked under a bunch of them. I think if I figured out, five or--if you count the acting ones--seven or eight different commissioners in the eleven and one-half years that I was the bureau director.

RO: Well, you came in under Dr. Goddard.

CV: Dr. Goddard and Mr. Rankin. And Dr. Ley was a fine man to work with. Dr. Edwards, I think, was the best I worked with.

RO: Did they had different administrative styles?

CV: Yes. Edwards was such a personable fellow. He didn't get all hung up in all the details. I think Schmidt's attempt to make a unit out of the Food and Drug Administration through those long meetings--what did he call them?

RO: Policy boards.

CV: . . . policy board meetings, was about the worst experience we ever had. And I think his objective was real worthwhile. I remember once he said, "I want Food and Drug to be something more than a group of bureaus tied together by a parking lot." And that's a good objective, but we sat there for hour after hour talking about some of those regulations that we couldn't care less about, and maybe should have but, you know, we had our own problems.

RO: Speaking of Dr. Schmidt, it reminds me, we haven't talked about recycled animal waste. Dr. Schmidt was commissioner when the agency was concerned with what to do about using chicken litter in animal feed.

CV: Yes, that's a good one. Mr. Hutt was insisting it had to be a food additive application. And I said, "Peter, when you go before a congressional committee and say that chicken shit is food additive application, I don't want to be there. You may be there all by yourself." That didn't deter him. That got resolved very pragmatically, didn't it? The states kind of took over; there's nothing particularly wrong with it. I have no idea how much chicken litter was being used for feed, do you?

RO: No, I don't remember. I remember on a trip one time we made down into North Carolina. I'm not so sure where else too.

CV: Virginia, yes.

RO: But that raised the problem of drug residues that have been fed to those chickens, and we were now going to recycle all of those residues.

CV: But Ron, that's an interesting point, and I think the answer to a lot of those problems is the dilution is the solution. Now Bill Bixler got all hung up about meat scrap and tankage from animals that were contaminated with pesticide or chemicals like that. And I said, "Bill, what do you do with them if you don't put them through the rendering plant?" "Bury them." I said, "No."

Here's a dairyman in southern Arizona; it's 110 degrees, and you've got 400 dead dairy cattle contaminated with pesticide, and you are going to bury them? You can't, you know. It's just so impractical. Well, there are very few small rendering plants in the country any more. They're almost really big now. So you put through one lot of cattle with a slight residue, and it get's mixed with all the other stuff that's coming out of that plant. Then the fact that those ingredients are used at a very low level of the total feed ration. That's why I said dilution is the solution. And I think that's a very sound concept. It's the same thing for the chemicals that wash into the rivers. You finally get to whether it's not enough to make any difference.

Let's say there was a little residue in the meat scrap or tankage you fed to some pigs. Then the dilution again when that becomes food from those pigs is going to be another whole order of magnitude. I don't think you could ever detect it.

And we talked about salmonella just a little bit, but I remember once that the Bureau of Foods people were going to get all the salmonella out of animal feed, and then you see them unload fishmeal with front-end loaders on big tractors in the holds of ships. And then those tankage people and meat scrap people will tell you, "Well, you know, we get the worst cars the railroads have got. They're all contaminated when we get them." When they ship them there isn't a cover over the car. So the birds are roosting all over these cars while they're standing in the yard--you can't keep that feed sterile.

RO: I think eliminating salmonella from the food chain was when Goddard came in. That was coming from his background.

CV: CDC.

RO: Yes. It's not even possible . . .

CV: Bixler was hepped on that. I believe it's going through another recycle right now, isn't it?

RO: Well, I know that they're concerned about it.

CV: Well, aren't they talking about another program again?

RO: Could be, but I could give them some first hand experience.

CV: Yes, I could too. And there were some of those plants that they could never get cleaned up. You had some of that, too, didn't you?

RO: Oh, sure.

CV: You could never get them to produce sterile products.

RO: I remember there was one big importer of fishmeal, and he was going to run all the fishmeal through a sterilizer. Well, the poor fellow ended up with a contaminated process there, so that all the fishmeal that came in on the boat that didn't show any evidence of salmonella came out the other end with salmonella.

CV: And then that PCB incident was a matter of trying to terminally heat that product, and they got the PCB in the meal, and it was ten times worse than the salmonella would ever have been.

RO: Well, Don.

CV: Well, I think I've spent lots of your time.

RO: I appreciate all the time that you've spent. Is there anything else you'd like to add then?

CV: No, I don't think there is. I have no regrets for the years I spent working for Food and Drug. I felt at one time that I was being unjustly accused. I guess Mr. Hutt gave me a kind of backhanded compliment in one of those hearing reports. He said I'd have been a good executive secretary for a livestock association. (Laughter) I always was concerned about the economic end. Coming from a farm background, farming is not, you know, a great big wonderful deal. Usually operating on a pretty close margin, and I think they ought to have every advantage they can get.

RO: When you went to the Pork Producers Association, did you have much direct contact with FDA on that?

CV: No, I was very careful to observe those rules. No direct contact for the first year with anything we'd been directly involved in. Mr. Gardner warned me about that one time, and I told him I was very well aware of those rules. It was a coincidence how many things the pork producers were interested in that I had been involved in. We mentioned nitrates, antibiotics and feed, sulfonamides: all of those things I'd been involved in. But I didn't go directly, of course. That was verboten. I forget the rules now, but then I tried to be sure I observed the rules.

RO: Well, Don, thank you very much.

CV: Yes, you're welcome.

(Interruption)