

History
of the
U.S. Food and Drug Administration

Interviewee: Andrew J. Beaulieu, DVM

Interviewer: Suzanne W. Junod, Ph.D.

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Interview with Andrew J. Beaulieu

April 16, 2010

TAPE 1, SIDE A

RT: This is another in the series of FDA oral history interviews. Today, April 16, 2010 we're interviewing Andrew J. Beaulieu, a veterinary medical doctor. The interview is taking place in the Parklawn Building in Rockville. The interview is being conducted by Dr. Suzanne Junod and Robert Tucker.

Doctor, we could begin, if you will, with a brief background, personal and educational, and then move into any experience you might have had career-wise prior to FDA that may have led to your interest in FDA or related to your work later with the Food and Drug Administration, and then go into some of your career experiences.

To the extent we can, we would like to recover some of the early history of the Bureau and then Center, and move forward to the present time.

So, Doctor, with that, we'll let you begin.

AJB: I was born in Washington, D.C., in April 1943, lived in D.C., 17th and C Street, N.E. for about six years, and then the whole family moved out to Silver Spring,

Maryland. And I did all my schooling, public schooling, there through high school.

I went to the University of Maryland for a couple of years on and off, finally got serious about college in 1964, and went down to the University of Miami in Florida; graduated from the University of Miami with two bachelor's degrees, one in biology, one in chemistry, B.S. and B.A., in 1967. Got married that summer. Went back to Miami on a [unclear] fellowship in cellular and molecular biology to start work on a Ph.D. Put in about a year on that Ph.D. program, decided that wasn't exactly what I wanted. I wanted to be closer to working with animals than I would be in that program.

So my wife and I decided to go out to Ohio State. She wanted to pursue her master of arts, and I decided to go to vet school, so we both went out to Ohio State. She got her master's degree there at Ohio State and taught for a couple of years. I got my doctor of veterinary medicine degree and was all ready to stay at the Ohio State University for a Ph.D. there in pathology -- they had a teaching fellowship in pathology there -- when Julie got, my wife got an offer to work at the National Gallery, which was really a nice offer. And so I started exploring the

possibility of coming back and working for the government, in particular with the FDA.

And I think I was interested in the FDA because when we were growing up in Silver Spring, our backyard neighbor, across the back fence, was a chemist that worked at the Bureau of Foods, and he'd recounted his experience at the FDA and it always impressed me that . . . I was a '60s liberal and fond of President Kennedy and so on, and so, I mean, the whole purpose of the agency and my philosophy sort of meshed, and so I was interested in FDA.

And one of the regional veterinarians out in Ohio, Homer Schmidt, came. He interviewed me and explained the nature of the job and so on, and it sounded interesting, so I applied for it. And I didn't know it at the time, and we can talk about it a little bit more later, but the Center, the whole agency, I guess, at that point, but the Center was in the process of a major hire-up. So I got offered a job pretty quickly and started working in the Center in June of 1972.

RT: Was Dr. Smith, he was a veterinarian?

AJB: He was a regional veterinary medical officer.

RT: I remember him, and I was trying to remember his first name.

AJB: I think it was Homer Smith.

RT: Yeah. And I think at that time you were quartered down in Temple D or Temple C. It was a small staff at that time.

AJB: It could have been. When I got to the agency, the Center -- the Bureau then, not the Center -- the Bureau of Veterinary Medicine was located in this building, the Parklawn Building, on the sixth floor. I heard from folks that I was working with at that time that had gotten there a little bit ahead of me -- and most of the people I was working with hadn't been with the agency all that long, and a lot of them had come over from USDA during that big hire-up. But they had been working at Crystal City, I think, before they came over here, and a lot of them had bought houses over there in Virginia because they'd relatively recently moved into the agency, and then no sooner did they buy houses than they got moved to Maryland.

RT: Yes, I know about that because when I first reported, we were in HEW North, and within that week we moved into Temple D, where I met and knew Dr. Smith, and we moved to Crystal and so on. And I also bought a home in Virginia and decided to stay there, so I'd commute.

AJB: Most of the folks did, yes. And I guess the commute wasn't as bad then as it . . .

SJ: Kind of like living here in Rockville and commuting to White Oak.

AJB: Yeah.

RT: Well, that's interesting.

Now, at the time you joined, Doctor, was it still a Bureau?

AJB: Absolutely.

RT: It wasn't a Center yet.

AJB: No. I don't think we became a Center until 1984.

I went back and did a little -- I heard a lot from folks that were here at the time I came in, but in light of this interview, I went back and did a little digging and refreshed my memory on some of the earlier history of not only the agency, but how the Center came to be a Center. And, of course, folks like to think -- I guess I did for a long time -- that the agency came, basically the Food and Drug Administration came into existence in 1906, when the Pure Food and Drug Act was passed, but that's not really true. The responsibility of birthing the 1906 Act went to the Division of Chemistry in USDA.

RT: That's correct.

AJB: And, as I understand it, the first organization that was called the Food and Drug Administration didn't come into existence within USDA until about 1930 or so.

[Recorder turned off and on]

RT: Well, let's see, Doctor. The Bureau then had its beginnings early in the '30s in the Food and Drug Administration. You were going to speak to that, I think, when we interrupted for a moment.

AJB: Yeah. And my understanding is that what became an organization titled the same way that we are now titled came into existence in maybe 1930, and then that organization moved out of USDA into the Federal Security Agency in 1940.

There were a lot of amendments to the statute along the way, but clearly the biggest one was the 1938. That's when the statute as we currently know it, the Food, Drug and Cosmetic Act, [unclear] really came into existence. And it significantly increased the authority of the agency to regulate drug products and a number of other products. And the big change sort of in principle was that products, drug products, should no longer get on the market until they were approved by the agency, determined by the agency to be safe, before they went on the market.

And my understanding is that folks on the Hill had been trying to give the agency this authority for some period of time, without a lot of success, because then, as now, I suspect, the pharmaceutical industry and other folks that were in the process who would be regulated weren't anxious to have that happen, and they had a lot of clout. That maybe wouldn't have happened in 1938 if it hadn't been for Beech [sp.] and Massengill, or maybe it was just Massengill at that point, going on the market with elixir of sulfanilamide and killing over a hundred people, most of them children. That catastrophe really is what I think provided the impetus for Congress to finally pass the Food, Drug and Cosmetic Act in 1938.

I guess the next, in my view the next major thing that happened to the Act after that was maybe the Durham-Humphrey Amendment of 1951, which formally established and described that class of drugs that could not be marketed unless they were marketed with a prescription legend on them. Both of those, I mean, obviously those two things would ultimately affect the way the Center did its business.

RT: Well, of course, the Humphrey Amendment was really related mostly to human drugs.

AJB: It was. We established, we did essentially the same thing by regulation that the Humphrey-Durham Act or Durham-Humphrey Act did by legislation. And there was always some question about the legality, and that led to that regulation subsequently -- we'll get there -- being given the force of statute later on by an amendment to the [inaudible].

RT: I think animal health -- I forget the exact title of it . . .

AJB: I think, actually, AMDUCA did that, the Animal Medicinal Drug Use Clarification Act, I think.

RT: Yes.

SJ: What date was that?

AJB: That would have been in 1994.

SJ: Yeah. I thought it was very late.

AJB: It took that long for it to be formalized.

But then, in 1953, the Federal Security Agency went into DHEW, and we went with them, and so the agency has been part of the Department, now HHS, since that time.

And probably associated with the fact that the organization changed its basic leadership or who it reported to, in the following year FDA was reorganized, once it got a new home, into five bureaus, and one of those bureaus was the Bureau of Medicine. And within the Bureau

of Medicine, for the first time there was an organization formed which was dedicated to veterinary medicine.

RT: And that was really at the Division of Veterinary Medicine.

AJB: Actually, initially I think it was a Branch. I have no idea how many people that had, but typically a Branch didn't have more than a half-dozen people or so, so it was a pretty small organization in '54.

And then a major thing happened, a major amendment to the statute that dramatically affected what was then the Branch of Veterinary Medicine, and that was the passage of the Food Additive Amendments in 1958.

So, for the first time, all those substances that were going into animal feed were clearly covered by a new requirement, and the requirement for animal feeds, animal feeds being foods because food is food for man or other animals, they were subject to the same requirements as any other food additives. And, at the same time, it became very clear that not only were the substances that went into animal feed food additives, but the drugs that went into food-producing animals were now food additives and clearly had to meet the same standard. That standard included the Delaney Clause.

So, a significant, a major responsibility then fell on the then-Branch of Veterinary Medicine, and in the following year the Branch became a Division within the Bureau of Medicine.

RT: I think at that point, one of our interviews -- I think the Van Houweling -- said that when he took over, there was 121 persons on the staff. So, since that time, obviously, there's been an expansion of staff and resources greatly forward.

AJB: Yes, fairly dramatic. I'm surprised that it was as big as 121, to tell you the truth, when Van Houweling took over. But clearly the organization, ever since 1958, the organization has been growing significantly.

The next thing that happened was the Kefauver-Harris Amendments in 1962. That added a whole 'nother set, gave the agency a lot more authority, which was fine. Sort of the other side of that coin is it gave the agency a lot more responsibility, more mandates to meet, and so it needed more people to do it. And that's another interesting, I mean, Kefauver-Harris, as I understand it, again, they'd been trying to increase the agency's authority for some period of time without success, and it probably, thalidomide and all the associated press and everything probably helped push Kefauver-Harris through to

passage. But it seems like a major amendment of that floor at least, it almost takes a catastrophe in order for Congress to do what it needs to do.

Kefauver-Harris increased the agency's authority in a lot of ways. We tend to think of it as the effectiveness portion of the statute, which it clearly was, but it did a lot of other things. It increased our inspection authority. It increased our authority over investigational drugs dramatically. It required, for the first time, sponsors of approved applications to report post-approval adverse reaction information [unclear], a major increase in responsibility. And that, along with it, required basically that the Division within the Bureau of Medicine become a Bureau in its own right, and that's what happened in 1965. So that's the first time that we were an independent organization within the Food and Drug Administration, was in 1965. And I think Dr. . . .

SJ: I've had that date, but I didn't think there were that many people there, so I'm a little confused [unclear] not right.

AJB: Well, Van Houweling came in in 1967, and I think that, January of '67, and that's why I was a little surprised that there could be as many as 121 people on

board when he came in. He could very well be right. I don't know.

SJ: Well, my notes have that the first veterinarian was hired in 1965. That couldn't possibly be true with 125 people.

AJB: No.

SJ: So something's not right there. Well, good. We can get the record [unclear].

AJB: Yeah. I think, well, there were veterinarians performing work similar to the kind of work that the Bureau does now and the Center does now way early. In fact, I think Dr. [Henry] Moskey was hired way back in the Bureau of Chemistry in USDA, maybe the first veterinarian doing that kind of work.

But the first vet, Dr. Collins was the Branch Chief essentially when we were branching medicine. Dr. Durbin was the first Division Director. Dr. [Bob] Clarkson was the first Bureau Director, but he was only here for -- that's pretty unclear as far as I can tell. He was only here for a matter of months. He was the former president of the American Veterinary Medical Association. They wanted somebody with a lot of prestige to be the first Bureau Director. He agreed to do that, but after agreeing to do that and being here for a few months, the AVMA

offered him a permanent position as the Executive Secretary of the AVMA. He took that job.

That left the Bureau Director position open, with an Acting Director, between sometime, apparently relatively early in 1966, when Dr. Clarkson left, until January 1967, when Dr. Van Houweling showed up. And Dr. Van Houweling was the Center Director for about 11 years, until 1978.

And just to sort of fall in along that line, then Dr. Crawford took over as the Bureau Director, I should say, at that time, and he served . . . Funny, he served in sort of two terms with about a year and a half in between. He served from '78 to '80. Then he left for about a year and a half. I can't remember now what he left to do, but he came back in '82 and served till '85. It was during that period from '82 to '85 that the name of the Bureau was changed to the Center for Veterinary Medicine, along with all the other bureaus in the agency. They all changed to Centers at that point.

SJ: They wanted to keep Dr. Parkman, the famous [unclear] physicians, and they couldn't pay him more money, so he demanded that his Bureau be renamed a Center, and, naturally, everybody else followed suit.

AJB: Is that what the basis for that was?

SJ: They wanted to be more, less bureaucratic and more along the lines of an [unclear], more scientific.

AJB: Right. That was the reason I heard, is they got tired of being, they didn't want to be called bureaucrats anymore, so they became Centers.

SJ: Dr. Park got that as a perk.

AJB: Ah, that's interesting. I'm happy to know that.

Dr. -- I mean, just to follow down the directorships a bit -- Dr. [Gerald] Guest had served in that Acting between that period when Dr. Crawford was here and not here. He became Dr. Crawford's deputy when he came back the second time, and he became the Center Director when Dr. Crawford left. So Dr. Guest was the Center Director from '86 to '93, and Dr. [Steven] Sundloff came in in, I guess early '94, actually.

RT: What was the last name?

AJB: Sundloff or Guest?

RT: Pardon?

AJB: Which one? Dr. Guest or Dr. Sundloff?

RT: The last one.

AJB: Yes, Steven Sundloff. And he was actually Director for 14 years. That's the longest tenure of any director. And he left in 2008 to assume the directorship of the Center for Food Safety and Applied Nutrition. And

Dr. Dunham, who had been his deputy, took over as Center Director at that point, and she still is.

But that sort of brings us up to date on the structure of the organization, how it came to be a Center.

I'm not exactly -- I tried to find out and couldn't immediately. I would have thought it would have been online somewhere, but we're well over 400 people now, I think. What with user fees and everything, there's been a lot of hiring going on, so . . . We're probably still the smallest Center, but we're getting there.

RT: Well, there was a period during the time we've been discussing where the clearance of medicated feed applications, for example, or drugs for medicating animals, had to be cleared both as a food additive and as a drug.

AJB: Yeah, that's right. And I think that was the primary reason for the biggest change from the Center for Veterinary Medicine standpoint, and the statute was the 1968 Animal Drug Amendment.

RT: Yes.

AJB: And the primary reason for that, I think, was exactly that. Up to that point, animal drugs had to be, or at least those that were intended for use in food animals, had to be approved both as drugs under 505 of the statute and as food additives under 409 of the statute. And the

requirements weren't always completely consistent, so not only was it cumbersome to go through two approval processes, in some cases it led to situations where it was difficult to approve things under both, to meet both standards.

RT: I'm sure that was a real problem for the industry to deal with, two separate entities.

AJB: Yeah, right. And this was, I think this was one change in the statute that the industry thoroughly supported. So in 1968, 512 of the statute came into existence.

It's interesting, though, that 512 incorporated almost all of the same standards that had previously existed. Where there were conflicts, I think those were resolved, but basically, with respect to food safety, the standards of the, the food-additive standards were essentially put into 512. Where it came to animal safety and effectiveness, the human-drug standards of 505 were put into effect. So the standards really didn't change a whole lot. It was just clear that they now only had, there was only one application process that anybody had to go through to get an animal drug legally on the market.

RT: So that probably expedited the time involved, too, did it not?

AJB: That was certainly the hope, and I assume that it had some beneficial effect. But the industry I don't think, ever since I've been in the Center since '72, maybe up to the point where user fees came into existence and then started to be implemented and have a real effect, I can't recall a time when the industry was ever satisfied that we were approving drugs fast enough.

RT: Well usually when they find it's advantageous to doing business and so on, that they are very supportive. But when it's extra regulation *per se*, that's not what . . .

AJB: That's right, that's right.

So, I mean, I think there was already a significant amount of hiring-up after '58, '62, and then the Center, but the Bureau became a Bureau in '65. If they had reached 121 by the time Dr. Van Houweling came in, then obviously a lot of hiring had been going on. But it continued, certainly, up to the point where I think that wave of hiring, I might have been on or near the tail-end of it, but it continued for another two or three years, I think, after I got here. So it was just a huge increase in the size of the Bureau around that time. And I think, even with that increase, I'm not sure that he ever had enough people to adequately implement all those changes to the

statute that had taken place over that relatively brief period of time, from '58 to '68.

RT: You touched on the matter of user fees. Now, does the Center now have user-fee authority, and for what applications or . . .

AJB: We originally got user-fee authority for essentially what you'd call pioneer applications, not generics. They didn't want to be part of that process at that point. We got it in 2003. The Animal Drug User Fee Act passed in that year, and like, by that time, human drugs had had user fees since 1992, I think, so they were on their third round of re-upping for user fees while we were still working on our first. And I think we tried hard; we were really trying hard to get them both, both ours authorized and theirs reauthorized in the same year, 2002. But the generic drug industry stepped in in the very end of that process, scotched the process, so we didn't get user fees in 2002 like we wanted to, but we got them the following year.

The generic, we did our first -- I'm not sure what they call it -- re-up, but basically renewal of the user fees in 2008. And by that time, essentially, the generic drug industry had decided that wasn't such a bad idea after all. I mean, it was really working pretty well for the

pioneer guys. So they decided they wanted to play that game too, and now we've got an act, an amendment to the statute. The Animal Generic Drug User Fee Act was passed, so we now have generic drugs covered user fees as well.

And from the beginning, within the agency itself and within the Center, there's been a lot of argument both ways as to whether user fees are the way to go for a regulatory agency. To what extent would it make you either beholden to the industry or appear to be beholden to the industry? And there are some sort of, well, as long as we're not more than 50 percent supported by user fees, then we can argue we're still pretty independent.

And so the agency may, as far as human drugs are concerned, that might be approaching that number. I'm not sure what our percentage is, but it's not that close.

And the way it was implemented, we pretty much copied all the administrative processes that had been set up by the agency for human drugs. And the folks out on the floor, the money, it's totally transparent. They don't see any of that, they don't deal with any of that, so there's no feeling that I've ever run into that any decision that's being made is being directly affected by the fact that user fees are in existence.

What has had a significant impact, and people would argue that it should -- that was part of the purpose of it -- was that the deadlines associated with the user fees, targets that were set as a condition of industry paying those fees, are taken very, very seriously within the Center of Veterinary Medicine as well as elsewhere in the agency, and so folks feel pressured to do things on time.

Now, my sense is that the resources that the Center has gotten based on user fees have been sufficient to allow people to meet those timeframes without major stress. Some of the folks that are involved in that process might say differently, but my general sense is that we've calculated the resources pretty well so that folks can do their job within those timeframes, do a good, thorough job.

Other things have happened during this period of time. One of those is really significant, and it happened just about the time I got to the Center, which have affected the number of applications, new animal drug applications coming into the Center. And user fees are calculated, the fee per application depends on how many applications you get. So our user fee applications, the application fee has gone up fairly dramatically over the course of time from 2003 to the present time, and the industry is not happy about that.

But what primarily caused that decrease was the issue of antimicrobial resistance, and that's been, as I say, that issue has been with the Center almost since I came into it. We published, the Center published *Federal Register* notices and regulations in the early '70s, I think, '71, '73, which required that all antimicrobials basically used in animal feed be subject to an additional set of requirements for approval dealing with whether they enhanced the resistance of microorganisms in a way that presented a hazard to human health. It's been extremely difficult for the Center to deal with that issue because it puts, arguably, the welfare of animals and the welfare of humans in conflict with one another. What's more important? Ensuring absolutely that there's no risk associated with the impact of the use of antibiotics in animals on humans? Arguably, the only way you could probably accomplish that would be never to approve another antibiotic in animals, but that would create all kinds of health risks for humans associated with not using them. And so you have to, striking that balance has been extremely difficult for the Center, and it's still a major issue.

SJ: Well, when you came to the Center, what were you doing?

AJB: I came into the Center as a new animal-drug reviewer in what was then the Division of New Animal Drugs. That would be the equivalent now of the Office of New Animal Drug Evaluation, a lot smaller organization then. And I was in what was called the Anti-Parasitic Drugs Branch. We did all the enfontic [sp.] applications, flea collars and stuff like that, [unclear] and so on. We did all those applications.

And I was in that office for probably a year and a half or so when the Center was -- I think it was a good idea -- the Center was doing rotations. And so like, say, for a year we're going to swap; you two guys are going to swap jobs. And so I went up to work in Compliance, the surveillance and compliance portion of the Center, and somebody else came down and swapped jobs. By the end of the year, we both liked where we were to the point where they made the swap permanent. So I ended up, for the next 15 years or so, working largely in the surveillance and compliance area of the Center, up to the point where I became the Director of the Division of Surveillance.

SJ: And what was the job?

AJB: That Division was responsible, then and now, primarily for assessing all of the information that came in from sponsors after a drug was approved to try to make a

determination of whether it was actually as safe and effective as we thought it was going to be when we approved it in the first place. You make those decisions on a solid basis of data, but it's still a relatively small population of investigational animals. You're never quite, you're never a hundred percent sure how it's going to work in the marketplace.

RT: In the veterinary organization have a program somewhat similar to the human drugs where they trace -- well, in human drugs, I think they call it adverse reactions, where you get reporting back, clinical experiences.

AJB: Absolutely. And that's exactly what -- that was one of the primary functions of the Division of Surveillance, was to monitor all those adverse effects, all the promotional material for products once they were out there on the market and so on, the stability of the drugs. All that information came in on an annual basis, and those reports were streaming into the Division of Surveillance.

The other major function of the Division of Surveillance was to provide the scientific technical support for all of the regulatory actions that were taken by the Center, so all of the compliance actions that went forward, virtually all, the technical support for those,

scientific support for those actions, was provided by the Division of Surveillance. The chemists, if it was a GMP case, the chemists in the Division of Surveillance provided the expertise to support those cases. If it was, for instance, a new illegal marketing of a new animal drug case, which a lot of our cases were -- people went on the market with animal drugs that should have been [unclear] approval and just weren't, and they just started marketing them -- and we want to take action to get that product off the market unless it got an approval. We had to provide the expertise to support those cases. And usually, when those cases went to court, we had to get outside experts to support us. That was part of our function too.

RT: Do you have representation of the Office of General Counsel that handles veterinary regulatory matters?

AJB: Yeah. Never, over the whole course of my career there, never enough, in our judgment, never enough OCC support. But, yeah, there have always been more than one OCC attorney who was assigned to the Center. And I guess they have litigators. If it gets down to the specific case, you might draw a litigator from their pool of litigators. But there are always regulatory counsel in OCC whose primary function was directed to CVM, and they were the ones that reviewed all of our guidance documents, any

regulation we wanted to write, *Federal Register* notice we wanted to put out and so on, they were the ones that . . .

Now, what's happened more recently is that a lot of attorneys that were in OCC have moved into the Centers, so the Center now has regulatory counsel within the Center that, a number of them have had experience in OCC before they came to the Center. And so a lot of the advice we used to get sort of informally from OCC, we now get from the folks that, the attorneys that are sitting inside CVM itself, and when we get to some formal clearance that's required, of course, that still goes to OCC.

RT: Have there been any major areas of regulatory action, any particular type of products that have been more of a regulatory problem than others?

AJB: Well, there was a whole period, largely during Dr. -- well, it peaked, I should say -- during Dr. Crawford's tenure, so between, say, '80 and '85, there was a lot of illegal distribution of prescription drugs. They weren't being sold by prescription; they were just being sold essentially over-the-counter. And there was a lot of litigation against folks that were doing that. It still happens. We just don't have enough resources to do as good a job there as we should.

But another thing that was happening was that completely illegal sources of veterinary drugs, and some of them of serious public health concern, like chloramphenicol, were being sold on a bulk basis in the United States largely for use in food-producing animals for which they weren't approved. Nobody knew what the appropriate withdrawal period was. In the case of chloramphenicol, there was -- it's rarely . . . It's used in humans only as a last resort because it produces, in a small percentage of folks exposed to it, a fatal aplastic anemia. I mean, you don't use chloramphenicol in people unless there's nothing else that's going to work. It's a last-resort drug. But it was very effective for use in cattle particularly, and so people were using bulk chloramphenicol shipped in from China or Yugoslavia, or wherever, in cattle.

SJ: Do cattle even get aplastic anemia?

AJB: It's not a problem for the cattle.

SJ: I was going to say.

AJB: But it's not a dose-related, as far as they can tell, it's not a dose-related response.

SJ: With the chloramphenicol, right?

AJB: Exactly. So if there were any chloramphenicol in the tissues of those animals after treatment, that poses a huge public health risk.

The other thing about that was, not only were they And that produced a lot of bulk drug cases. The Department of Justice took action against a number of veterinarians and others out there that were distributing bulk drugs, and I think they turned that around to a considerable extent.

But the other problem with chloramphenicol was that there was an approved product, an approved source of chloramphenicol, for dogs, and that product was being used extra-labelly by veterinarians in food-producing animals.

SJ: What would it have been approved for?

AJB: It was approved as an antimicrobial in dogs, I think, for urinary-tract infections and other things.

SJ: And dogs also are not subject to aplastic anemia.

AJB: It was not a problem in dogs, right, as far as the primary

SJ: And we don't eat dogs.

AJB: We don't eat dogs.

So its approved use wasn't a problem, except that, over the years, manufacturers, probably recognizing that it

would be a good drug to use if they could ever get it approved, which they didn't think they could, in food-producing animals, they started putting it out in larger and larger dosage sizes for dogs, to the point where I think finally there was a thousand cc vials, injectable, approved, and boluses for like 150-pound dogs were approved, which made it really nice to treat calves and so on with. And so those products were clearly being used for purposes in food animals that they weren't intended to be used in.

SJ: And you can investigate how much was being produced and how much . . .

AJB: We could.

SJ: [unclear] and extrapolate on how much could reasonably be used in a dog population.

AJB: Right. And we did two things at that point. We published a notice proposing to withdraw the products involved, at least those that were the larger sizes and so on. And we proposed to enforce a provision of the statute which we had never sought to impose before. And there's a section of 512 that says that a product cannot be legally manufactured, distributed, or used by veterinarians in this country unless that use was approved by the Food and Drug Administration. So unlike 505, which permits physicians to

use any drug they can obtain any way they want to -- I mean, extra-label use was a routine part of clinical practice for physicians -- read literally, and appropriately, I think, the Center for Veterinary Medicine was in a position to tell veterinarians they could not legally use chloramphenicol in an extra-label fashion. We took, we made the decision to impose on their ability to practice medicine the way they wanted to, because their practice of medicine was potentially adulterating the animals, the food supply that was coming from those animals. Well, you can imagine the way the veterinary profession reacted to that.

So what we did was we said, "That is the law, and technically, that is the way the law should be enforced, that is the way we choose to enforce the law with respect to chloramphenicol. If we catch any veterinarians using it in food animals, we are going to put you in jail." I don't know that we ever actually -- we did put a veterinarian in jail for chloramphenicol, but it was primarily associated with bulk drug administration, not extra-label use. But it became clear that we were serious about that, and I think we largely curtailed the use of chloramphenicol in food animals.

SJ: Give me a time frame.

AJB: Again, this was happening during Dr. Crawford's tenure, so it was sometime between '80 and '85 that we were doing these kinds of things.

But we did not want to totally prevent veterinarians from using approved products in an extra-label manner, certainly not in companion animals, for instance.

RT: Now, there was an act that probably relates to what you're moving to now. That was the Animal Medicated Medicinal Drug Use Clarification Act, which authorized veterinarians, in their professional judgment, to use extra-label.

AJB: Exactly.

RT: Probably outside of chloramphenicol, of course.

AJB: Yeah. What we did in the '80s was we established a Compliance Policy Guide which said, that is the law and we can enforce that provision of the law to the extent we choose to, and we choose to against chloramphenicol and some other products, nitrofurans, which are carcinogens, and a few other products that we were very concerned about.

We don't intend to -- we were going to exercise regulatory or enforcement discretion not to enforce that provision in the statute under certain circumstances: if

there was no other drug available, the life of the animal was threatened, yada-yada-yada.

Well, the agency and the profession worked under that Compliance Policy Guide, that exercise of discretion, for a number of years, and finally veterinarians -- I guess rightly, if I was in their position -- said, "Look, you've got us in the position now where we are routinely violating federal law in order to practice veterinary medicine. We want you to change the law and fix that," and that's what the Animal Medicinal Drug Use Clarification Act did.

Within those same kinds of parameters that we had established in the Compliance Policy Guide, the law said, within those parameters, and any others that the agency establishes by regulation, it is okay for veterinarians to

RT: Do you recall when that act was enacted?

AJB: That was 1994.

RT: Ninety-four.

AJB: Right. But it took some time.

SJ: Late.

AJB: Right. It took almost 10 years, I think, from when we first created the Compliance Policy Guide to actually essentially put that, the provisions of the

Compliance Policy Guide into the statute by virtue of the AMDCUA.

SJ: Before we move on to the small animals, which is [unclear], you were there during the imbroglio over DES in cattle.

AJB: Right.

SJ: And just -- you may not have been directly involved at all, but we're always looking for perspectives on one of the most visible regulatory, certainly in the public's eye anyway, the sort of embodiment of problems in veterinary medicine and crossovers into the human population.

AJB: Right. DES had been around for a long, long time, originally approved as a food additive. It existed long before 512 came into existence, and it was sort of grandfathered in under the new provisions.

But I can't remember the exact year, but it became clear that DES was a carcinogen, was a human carcinogen, and this was associated with the fact that it's actually been used therapeutically in some women as . . .

SJ: Allegedly therapeutically.

AJB: Yeah, okay, right. Again, it may have been an extra-label use that led to this. But the daughters of those women -- it was finally clearly established that the

daughters of those women had a relatively rare kind of vaginal cancer. And so, I mean, the Delaney Clause was pretty clear about what you could and couldn't do under those circumstances.

RT: Was that an adoneal [sp.] type cancer?

AJB: I think so. Yeah.

And I think things got complicated with carcinogens and regulation under 512 because, in 1962, the Delaney Clause was amended by the DES proviso to that clause, and I think to some extent it was probably one of those deals that gets struck, that somebody says, well, if you'll modify this portion of it, we won't contest, pass it through the law and so on, and so they got the DES proviso in, because it was pretty clear, even at that time, I mean, it was well known that at high enough doses, DES could be a carcinogen.

So the DES proviso says -- and this is one of those situations where lawyers write something and it makes perfect sense from the legal standpoint, but it makes almost no sense from the scientific standpoint. The argument is, well, okay, you can eliminate exposure of the public to the risk associated with a substance by never using the substance at all -- that's one approach -- or you can use the substance, and then you can make sure there's

no risk by assuring that there's no residues of that substance in the foods that the people subsequently eat. So the DES proviso says that's okay, you can use DES, or any carcinogen, for that matter, in animal feed or as a drug for animals provided you can establish that there's no residues of that substance in the food.

SJ: Or a pesticide in the food [unclear].

AJB: Yeah, exactly, and that came through, and the same proviso got applied there.

Well, the problem is, there's two problems, really, with that approach. One, what constitutes a carcinogen? I mean, does -- it's not a bright line as to when something is and isn't, so that's a matter of judgment in the first place as to whether something is even a carcinogen. But if it is determined to be a carcinogen, how do you decide there's nothing there? Whether there's something there or not depends on how hard you look. If you look by virtue of a method that's only got a two-part-per-million sensitivity, which is the method for DES at the time that provision was put into effect, you don't find anything. But if you look with a method that's got a one-part-per-billion sensitivity, you find something. So, that led to a whole series of, how do you define . . . And the DES proviso made it clear that the only method that counted was

the method that was acceptable to the Secretary, that is, to the Commissioner, really. So we set the standard for what the method would be. But how does an agency that's supposed to be protecting the public health with knowledge set a standard for the sensitivity of a method that's clearly, that you can clearly have a method that's much, much more sensitive than that, how do you maintain that as a regulatory method knowing there's another available? And that's the position the Center got itself into. We finally had to say the methodology is either [unclear] or they won't create the method we want them to create, so you don't have a regulatory method that's satisfactory; or we've used a method which we consider to be satisfactory, and using that method, we're finding residues. Therefore, it's got to come off the market.

We made an administrative error in that process. We published a notice that said we're withdrawing DES. We went through a hearing, sort of, and reached that point and said, "We're withdrawing DES," and DES came off the market. The manufacturer sued the agency and said, "You didn't follow appropriate administrative practice when you made that notice." The court said, "You're right, they didn't." So we had to . . .

SJ: Appropriate notice and comments?

AJB: Well, appropriate hearing process.

SJ: Hearing process.

AJB: Right, for the withdrawal. And so we had to go back through, essentially, the formal hearing process, which we might have actually denied them a hearing and gone to summary judgment when we shouldn't have. I can't remember the details. But in any event, we had to go through that process twice, and eventually the hearing was such, the hearing came out. The hearing law judge supported us, and we eventually got DES off the market.

SJ: Was there ever any evidence, was there even any study that whether it actually could . . . Well, you couldn't really do a controlled trial or anything. But was there ever any evidence that DES could transfer to humans and cause cancer? I guess, especially, since DES caused second-generation cancer.

AJB: Right.

SJ: I guess it was basically something impossible to study.

AJB: Right.

SJ: Is that correct?

AJB: And, for that matter, it wasn't important under Delaney to demonstrate that.

SJ: Exactly.

AJB: It was always there to demonstrate that it was a carcinogen and that it was there.

The conservative approach and probably even now the right approach is, we don't know what level of the drug it takes to cause cancer. Our argument is basically a sort of one-hit argument still, I think. Well, that's not true. But up to that point, at that point our argument was, it could take one molecule as far as we know. We don't know whether it causes the trigger cancer. So if we can find it, it's unacceptable.

And I can talk about, since we have mentioned a little bit, because we finally said, you can keep searching for zero forever. You can keep trying to increase the sensitivities and methods to some point where it simply doesn't make sense anymore. So we finally did say that if we can establish that the risk is no greater than to one person in a million people over the lifetime of exposure to this drug substance, that's zero as far as we're concerned.

SJ: And that was never questioned in the court like it was in the cases of colors, color additives?

AJB: We're enforcing in accordance with that requirement.

SJ: Okay.

AJB: Whether it was challenged and we won or whether it was not challenged, I'm not sure.

[recorder turned off and on]

RT: Okay. We stopped momentarily.

SJ: We were talking about sensitivity of methods.

AJB: Yeah. We were getting down to the point where methods were capable of measuring parts per trillion or even fractions of that. And the Center, and I guess the agency as a whole, decided that it needed to try to provide some risk-based assessment, some way to determine that functionally, there was a level which was of so little concern that it could be considered zero. And if we set the sensitivity of the method to that level, that risk-based level, and that's the level we chose to look for the substance at, if we didn't find any at that level, then there was no risk associated with whatever amount that might be below that. And that's, as I say, the sensitivity that we decided, the risk factor that we decided to accept -- and Dr. Crawford was heavily involved, when he was Commissioner, in this decision -- was one in a million. And there was one in 10 million and, you know, the people were trying to be more conservative.

SJ: Well, then that, too, was established very late.

AJB: Yup.

SJ: We're not talking that being established right after Delaney.

AJB: No, no, no, no. Ages went by, and we would have, you know, everybody was, we were still trying . . . Delaney gave us no choice. We had to keep pushing the method lower and lower and lower, and you got to the point where it was really difficult to validate a method at those levels of sensitivity to try to . . .

SJ: Have it reproducible.

AJB: Exactly. So that you could go to court and say.
. .

SJ: With some degree of confidence.

AJB: Exactly. That is a violative situation.

SJ: It sounds to me like foods got -- and I know in part that this is the case -- foods got involved in Delaney issues much sooner and in much more depth, so it sounds like after the color ruling about the one-in-some-trillion risk and the court said sorry, it said no, that's it. It sounds to me -- I'll have to check the dates, but it sounds like that was FDA's, CVM was the last response to that, and it sounds like it was allowed since that court decision was unworkable.

AJB: Yeah. I think another thing that got clarified, and I think the Center may have got to clarify this issue

too, was that Delaney was talking about primary carcinogens as opposed to secondary carcinogens.

SJ: Oh, the constituents issue.

AJB: Yeah. I mean, we had a substance, sulfonamides in general, and sulfamethazine in particular, which were known to cause thyroid hyperplasia, and at doses sufficient to cause thyroid hyperplasia, in a certain percent of cases that hyperplasia went on to become cancer. But the thyroid hyperplasia, we could never demonstrate that sulfamethazine or any other sulfonamides caused thyroid cancer without causing hyperplasia first, and that was a dose-related response. We could determine under the normal safety provisions of the statute that if you did not cause thyroid hyperplasia, you did not cause cancer. So, in other words, sulfamethazine was sort of a secondary carcinogen. If you could establish a no-effect level on the thyroid hyperplasia, then there was no risk of cancer, and so that's what we did. Now, we had to lower some of the tolerances that we previously published, but we established tolerances for -- and they were part-per-billion tolerances -- for sulfamethazine, and we escaped Delaney on the basis that no thyroid hyperplasia, no cancer.

And I'm not sure to what extent that provision, because we've been regulating, with the agency's blessing

and OCC's blessing for 15 years or more under that provision. In other words, we basically sidestepped Delaney and were simply applying the normal food-safety standards to sulfonamides. But it took us years of research in order to come to that conclusion.

One interesting thing about DES, during that whole process of getting DES off the market -- and there was a lot of concern about the safety of DES -- there were DES products on the market for companion animals at that point. We started taking action to get all those products off the market, in part because we were concerned about diversion of those products to human use. They didn't seem to have a problem, they weren't a problem in animals that we could determine, but they had never been proven to be safe and effective. They'd never gone through the approval process for animals.

SJ: What was the use for animals, for [unclear] use?

AJB: Yes. Estrus suppression in female dogs, among others, which was a useful thing.

SJ: Were there other things that could do that?

AJB: Yeah, that did not -- the veterinarians did not need to use DES for that purpose. There were other things that would accomplish it. So we took those products off the market.

TAPE 1, SIDE B - BLANK

TAPE 2, SIDE A

RT: This is a change of tapes. Okay.

AJB: Companion animal products that contained DES.

There were products that were specifically intended for use in dogs that contained only DES and were intended for so-called therapeutic purposes in dogs, and we started taking action against those.

It turned out there were also some vitamin-mineral preparations that threw a little DES in there and a little testosterone and a little thyroid hormone in there, and basically advertised those products for use in old dogs, made old dogs young.

SJ: Doggie quackery.

AJB: Yeah. And so one of the first court cases I ever got to go out on was a court case involving pet, a product called Pet Tabs G, which was, interestingly, marketed by Beech and Massengill. And Bob Spiller, one of the best litigators the agency ever had, was charged with DES cases. I mean, anything related to DES, he took at that time. So the first, my first experience going up to

court was with Bob Spiller, and that was -- if I ever needed validation, you know, why I came to work for FDA and what it was all about, that experience was it.

Bob was great. He was a wonderful attorney. He did not let it go unnoticed. One of our arguments with respect to taking this product off the market and requiring that it be an approved product in the first place, which it was not, was that it was -- they wanted to argue it had been on the market so long, it was grandfathered. And Bob Spiller pointed out that there were at least a dozen changes in this product that invalidated the grandfather argument. And among those changes were changes in various inactive ingredients. The formulation had changed in various ways. And so Bob was making the argument that it wasn't subject to the grandfather clause because of all these changes, and he had somebody on the stand from the firm that said, "Those are just, those are not important changes; they're just changes in the inactive ingredients."

SJ: Well, he just admitted the problem.

AJB: Bob Spiller goes, "Oh, so you're saying that inactive ingredients in a product are not something that we should be concerned about. Would that be inactive ingredients like ethylene glycol, for instance, in elixir

of sulfanilamide that your firm also produced and killed 100 people with?"

SJ: Oh my . . .

AJB: It's like, you know, you could just see . . .

SJ: The light bulb goes off.

AJB: The trap springs closed on the guy's leg.

And the judge, that, I mean, the judge, that tickled the judge so much that he started, he couldn't help himself, he started laughing. It was too classic. And, needless to say, we won that case handily.

But that was a terrific experience involving Bob Spiller and DES.

SJ: That's good. We hadn't gotten that before.

AJB: And so, yes, we took DES seriously. We got . . . You know, it's funny. You go, we got it off the market, and I had never heard, seen anything possible. Somewhere out there, somebody's still got some DES. But . . .

SJ: I'd like some Pet Tabs. I want somebody floating Pet Tabs around.

AJB: Yeah, Pet Tabs G, G for geriatric, I would think.

SJ: Geritol for dogs.

AJB: Yeah. That's basically, yeah, that's the kind of product that was supposed to make old dogs young.

I don't know. Other kinds of cases that we had.

I mentioned on the way in that we do not have, there is no pre-clearance requirement for veterinary devices as there are, as there is for human devices. But you cannot market a veterinary device that is misbranded in any way or that is adulterated by virtue of being unsafe. So, with respect to veterinary devices, we're in the position of basically, they get to put them on the market and then we've got to catch them. And we have taken action against a number of veterinary devices. These are because we could argue they were unsafe.

And in one case, in the case of anti-bark collars, they're audio activated anti-bark collars, the theory being that any time the dog barks, it would get a shock, and that would stop them from barking. The one we took action against went off for all kinds of reasons, a car backfired or the dog hit their dish when they were eating, and it would fire off for all kinds of reasons. And it was actually burning the dogs' necks. So we got that one off the market.

And there have been a number of just fraudulent things intended for horses and so on that we've taken actions as devices.

We don't have a cosmetic provision either, but we have things that sort of, that try to argue that they're grooming aids or cosmetics for animals that really have therapeutic claims on them, so we've taken some action on that basis.

RT: What kind of parts would you think of as cosmetic for veterinary use or . . .

AJB: Yeah. There are things that are sort of in the, I mean, there's any number of dog shampoos and grooming aids like that. But there are a lot of shampoos that contain insecticides and so on too. And that's another thing that's probably worth talking about.

CVM is, to some extent, like a small FDA in that it has responsibility for all the kinds of products that other parts of the agency have responsibility for that relate to animals. In other words, we regulate the animal equivalent of cosmetics or the animal equivalent of medical devices, as well as animal feeds. We regulate foods intended for animals as well as drugs intended for animals. So all the other product types that the agency regulates as an agency, we regulate as a Center.

RT: I thought it was interesting, one time I consulted with one of the veterinarians regarding a state official's inquiry, and I forgot which vet it was now, but

he said, "Well, as it stands now, nutritional labeling is better for pets than it is for humans." That was before, of course, the upgrade for human labeling, nutritional labeling.

AJB: Right.

RT: And that was kind of interesting. I don't know how that came about, really.

AJB: Because of concern for production animals and the need to know, to have a very clear idea of what the nutritional composition of various animal feeds was, I think that was part of it. A lot of states, I mean, they had their own control over that, and there was an Association of Feed Control Officials, and so on, that got together and collectively established standards for animal feed labeling, including pet food labeling.

RT: Well, I suppose that in part, too, it might have been fostered by fraudulent products.

AJB: Right, that too, yup.

SJ: And the fact that an animal, I mean, we eat a wide variety of foods and they're good. Dogs, some animals live exclusively on the feed.

AJB: Right. And that's their sole source of nutrition, so it's important that it be balanced right.

RT: And animal breeders would want to have healthy stock.

AJB: Absolutely, right.

But there are two confusing classes of products in terms of jurisdictional authority. Veterinary biologics are regulated by USDA, and drugs, well, products that have a therapeutic effect by virtue of eliminating fleas, for instance, are regulated by EPA under some circumstances but by FDA under other circumstances. But there are memos of understanding between USDA and FDA and FDA and EPA regarding which classes of animal products are going to be regulated by which agency, in other words, trying to draw a brighter line between these classes of products where there's arguably two agencies that could regulate the same class of products. And we got those pretty well worked out. If a product is intended to have its therapeutic effect by altering a specific immune process in the animal, then it's a biologic and would be regulated by USDA. If it doesn't operate through a specific immune process, then it's a drug that would be regulated by FDA, and we draw a fairly bright line between those two.

With respect to the pesticides, if it's a product that's administered orally to an animal, for instance, and therefore has to work systemically to accomplish its

intended effect, then we generally regulate that as a drug under FDA. If it's a product that's applied topically to the animal and simply is intended to kill the flea by virtue of having some direct action on the flea and not to have any action on the animal, then it's generally considered a pesticide regulated by EPA. Sometimes it's a little hard to distinguish between those two. So, flea collars now regulated by EPA, not FDA. Flea powders, flea shampoos . . .

SJ: [unclear] has effect on the environment?

AJB: Pesticides . . . EPA has the responsibility for pesticide registration in general, whether it's a pesticide use in the environment or on plants or . . .

SJ: And setting tolerances.

AJB: Yes. And whether it's a pesticide use on animals, including food-producing animals. So all those sprays for lice and ticks on cattle, EPA registers those products now. We do not approve those.

SJ: Okay.

AJB: So, and that's an issue that not everybody recognizes.

SJ: Kind of like cheese pizza versus pepperoni.

AJB: Yeah, right, exactly. There are some fairly hair-splitting distinctions about who's going to regulate

what. And we're still working on, and we're always working on refining those [unclear]. I think right now we're in pretty good shape.

SJ: Well, we've gotten away from your career. Maybe we can veer back into it a little bit.

Tell me about how you came to be director of OMUMS and what challenges you found and what fun you had, and what your contributions were.

AJB: Yup. Well, it's been interesting. I guess I did kind of have an interesting career path.

I mentioned the fact that shortly after I got here, within a year and a half or so, I moved from the sort of pre-clearance portion of the Center to the post-clearance and compliance portion of the Center, and I was in that position for 15 or more years, ultimately as a Division Director. Then, early in the 1990s, I think 1991, a division directorship opened up on the pre-clearance side again. There was a situation in which the director of that division sort of got himself into some hot water with respect to whether he was rigorously enforcing the pre-clearance provisions in a way that he should be. And so they wanted to move that person out of that position, and not only that, they wanted to make it very clear that whoever came in there was somebody that had a lot of

experience with compliance issues and so on, and so I was asked to take that position back on the pre-clearance side. I was happy where I was, but it turned out it was very interesting, and it got me into the management chain on the pre-clearance side of things, and probably a year or two in that Division Director position, and then I got asked to be an Associate Director in the Office of New Animal Drug Evaluation, which I was for a number of years, and acted periodically as the Director of that Office in the absence of the Director and so on.

And then a position opened up in the, basically the Deputy Director of the Center's position opened up, and I was persuaded by Dr. Sundloff, who was the Director at that point, to take the Deputy Director's position of the Center, which I did somewhat reluctantly. But Dr. Sundloff and I had agreed that the way we would establish the responsibility of the Director and Deputy Director position would be that the Deputy Director would be sort of the inside guy for the Center, and the Director would be the outside guy. He'd do most of the liaison with Parklawn and parties outside the agency, which he was very good at and liked to do, and which I was very bad at and didn't like to do, so it was a good fit. And so I went into the position on that basis.

But Dr. Henney and Linda Sevan [sp.] and others that were at the agency level at that point were really interested in doing some things at the agency level that required, in their judgment, more staff than they currently had. And so they basically started tapping the deputies of the Centers to perform, to get involved in all these agency-level issues. They were good issues. They just didn't have anything in particular to do with the Center for Veterinary Medicine and all the things I was interested in and good at. But I found myself outside the Center most of the time, over here in Parklawn doing things that I didn't want to do and wasn't particularly good at.

So finally I went to the Center Director. I said, "See, this just isn't going to work. I mean, this work does need to be done, but I'm just not the right person to do it. I'd rather be working inside the Center, as we discussed before." And he said, "Yeah, I understand that. So I became an Associate Director for Policy Issues, basically, within the Center, a step back from the Deputy Director position. Dr. Linda Tolleson [sp.], who was the Office Director at that time, then became the Deputy Center Director. She's a Commissioned Corps officer, since moved on to the Office of Women's Health at the agency level. She became the Deputy Director, and that was better for

everybody concerned, I believe. And I was in that policy position for really until the MUMS Act (The Minor Use and Minor Species Animal Health Act of 2004) passed.

And both when I was in [unclear] as an Associate Director, to some extent but not enough, when I was Deputy Center Director, and very much so when I was an Associate Director, I was working on getting the MUMS Act passed. It was the most important thing, in my judgment, that the Center could do because . . . Let me backtrack a little bit from the career to the more policy-oriented things.

The Center has a huge problem that nobody else in the agency has. They've got one species to deal with, to enforce the statutory provisions with respect to one species. We have to enforce the same statutory standards essentially with respect to thousands of species for which there are no approved drugs for most of those thousands species and never will be, because no one can afford to spend the money to get an approval for a product that's only going to be used in gerbils . . .

SJ: And chinchillas.

AJB: Right, exactly. It's just not gonna happen. Which means either those animals don't have any drugs at all, or you got it for extra-label use, which we did within reason. And even then, usually the formulations were such

that you couldn't use them in those animals very well, so you had to start compounding them, and you don't know what the hell is going to happen at that point. Or you had to come up with some other mechanism, some legal way to get some of these products on the market without the burden associated with a full approval. And that was the principal portion of the MUMS Act that I was interested in.

The MUMS Act came out of the Animal Drug Availability Act, which was passed in 1996. That Act was originally drafted by the industry essentially, on behalf -- Congress was technically drafting it, but in fact it was being written by the industry. The way they dealt with the problem of no product approved for minor species, or very few, was they basically said you don't have to demonstrate effectiveness for those products anymore. They just eliminated the effectiveness requirement, and we said that's not [inaudible]. That's not going to work. We're not taking that step backwards, thank you very much.

SJ: Not that.

AJB: And the point we made was, look, anytime you approve a therapeutic drug, there's always a risk-benefit determination that needs to be made. You can't eliminate one side of that equation entirely. We're willing to lower the bar for both of them to some extent so we can still

balance safety and effectiveness. And so what we did, we could take that provision out and put in there a provision that has Congress mandate the agency to study that situation and to come up with recommendations for further statutory changes if necessary to deal with that issue. So that's the way that Act was passed.

So that put the burden back on the agency to say, fix this problem, and we spent two years coming up with every kind of possible way that we could make life better for minor species in this country by allowing the drugs to be legally available, and we came up with three major changes.

One was, we picked up the orphan drug provisions, essentially, that had worked well for human drugs, and we put those in our statutes, and we now can designate animal drugs for minor use or minor species, so they get exclusivity provisions. Hopefully someday they'll get some of the tax incentives that they got on the human side. We haven't been able to do that yet, but we're working on it.

SJ: It's in research?

AJB: Right, exactly. So we can enhance the approval process. We can increase the incentives for somebody to actually go through the approval process. That's working quite well. We've got 80-some products at this point that have designations, and people are working on getting

approvals for particular intended uses on, including a bunch of minor uses, but anticancer drugs and things that firms weren't interested in going for until we got these provisions in effect. But they're working good.

The second was conditional approval. That was a process wherein you could demonstrate safety to the normal statutory standards, but you could delay the full demonstration of effectiveness while the product is being marketed. That's a process that had been applied on veterinary biologics and it seemed to work reasonably well, so we picked it up and used it for animal drugs. And we've got several products that are in the process of going through that process now.

And the third one, the big one as far as I'm concerned, was a completely new standard for getting products on the market, called indexing. You can -- they've got to meet certain standards up front. We can't have any significant environmental or food safety concerns. Basically, it's only for non-food animals. And they have to be able to manufacture it appropriately. If they can demonstrate that up front, and then they can get like three, a panel of three experts that are experts to our satisfaction to look at all the available evidence and conclude that, on balance, the benefit of this product for

its intended use offsets whatever risk there might be, then they can get that product legally on the market. And we've got a couple of those already through the process, and they're indexed, and there are a number more that are working on it.

But that's what I was interested in doing with my time, not spending it at the Parklawn Building doing other things. But it took until 2004, you know, from 1996, when we got 88A passed, to 2004 to actually get the MUMS Act passed.

SJ: It sounds like it needed a lot of crafting. You had some models, but it needed to be crafted in such a way to be specific to not only animal drugs, but specific to a small class of animal drugs.

AJB: And that third provision, the indexing provision, it was a huge fight to get that out, to get the rest of the agency to agree with it. I mean, I remember arguing with Bob Temple about that. "Oh, once you establish that standard for animals, we're [unclear]." I said, "Come on." A black molly in an aquarium is not a person. People can understand that you don't need to apply the same standard to black mollies and people. They tried to make that argument that if you could do it for black mollies, you can do it for people. It's just not gonna

fly. I mean, people can understand that. So, finally the agency agreed that we did not need to apply the same standard to black molly approval that we do for people approval.

SJ: Anyone that can take on Bob Temple with [unclear] argument, I will salute. He can out-talk me in . . .

AJB: Bob was a worthy adversary.

SJ: He always is.

AJB: Yes. But he's a fascinating person to deal with, and I enjoyed the interaction.

SJ: He always comes up with something you haven't thought of.

AJB: Right. I probably wouldn't have enjoyed it quite as much if we hadn't been successful, so, yeah.

But, yeah, we finally got, and there were other folks in the policy levels of the agency which had some concern about it too, but we managed to get it through.

The biggest hang-up -- it's going to be an issue forever, I think, for the Center -- was antimicrobial resistance. And Kennedy's staff was very concerned about that issue then, still are, I suppose, even in his absence, and they -- we were that close to getting it passed in 2003, and they stepped in at the final hour and scotched

it, and so we had to work on that and put some provisions in there to satisfy them. We weren't going to be using, we weren't going to be doing anything that would foster the use of antimicrobials to any extent greater than they already were, and so we finally got it passed in 2004. And I think that's the point at which I'd been kind of working toward, getting that law passed, and the law mandated -- and this wasn't my idea, actually; it was already in the provisions that Congress had put in the law.

And one of the provisions was that there would be an office created in the Center for Veterinary Medicine reporting directly to the Center Director that would deal with minor-use, minor-species issues. And when that office came into existence, well, actually, it got mandated, I went to Steve and I said, "Dr. Sundloff," I said, "that's my job. That's what I've been working toward all this time."

So, my career path went up to Deputy Center Director level, down to Associate Director, and then down to Office Director, so I said if I stay here long enough, I'll probably be a Branch Chief all over again. But I retired in 2007, got the job basically in 2004 after the passage of the MUMS Act and kept that job until 2007, when I retired.

During that period of time, we were writing implementing regulations, we had gotten two sets of proposed regulations, one for indexing, one for designation, out by the time I retired. And then, since I've been back as a consultant, we got both of those since finalized. And you've actually amended the designation regulations as a proposal and as a final [unclear], so I got that.

SJ: You were working with lawyers and chief counsel, or primarily in the Center until chief counsel kind of, at some point, had to get involved?

AJB: No. Laura Epstein primarily.

SJ: Oh, thank you. That's what I was hoping, yeah.

AJB: Laura Epstein, and she did a wonderful job.

SJ: Any other people you need to . . .

AJB: Well, everybody she worked with, you know, Ann Wyan [sp.] and on up, whoever happened to be chief counsel at the time. Ann was very helpful in writing the implementing regulations. I think Laura was the primary, and she had a lot of arguing to do within her own organization, but she was the person that really helped [unclear] for OCC.

SJ: Now, I should have asked this much earlier, but minor species does not include cats and dogs, I presume.

AJB: There are seven major species, have been for years and years by regulation, now . . .

SJ: Which are . . .

AJB: Dogs, cats, horses, cattle, pigs, chickens, and turkeys. Those are seven major species.

SJ: Okay.

AJB: Everything other than that is a minor specie.

SJ: Well, that's easy to define.

AJB: Yeah, and that's the way the statute defines it, by exception. It says, here are the major species; minor species is everything but those, and that's thousands and thousands of species. Now, obviously, not all of those species are ever going to need treatment, but lots of them do. All those species that are in zoos or public aquaria, all those species that are managed by the Wildlife Service, all those wild species, and a lot of those need drugs, if for no other reason to tranquilize them, to transport them, to whatever. None of those drugs, essentially none of those were approved.

SJ: Giant pandas.

AJB: Yup.

SJ: I'm sure you've had to do some inspections on that.

AJB: Yeah. Well, that's where -- I mean, extra-label use is absolutely essential for those animals, and we're going to get some of those products indexed. They're going to get legally on the market specifically labeled for some of these species now. But even if we can only get them indexed for, if we can only get them indexed for lions, for instance, and you don't get tigers, jaguars, and every other cat species, if folks have that product legally available for one, they're going to find ways to extra-label use it for others, and that'll be that.

RT: But this wasn't [unclear].

SJ: Doesn't sound like a public health hazard.

AJB: No, exactly, because it indexes only for non-food animals for all intents and purposes.

RT: Is research on the dosage or level of, shall we say, tranquilizer agents, is that a function of the industry, or is that also something that the Center would be interested in?

AJB: We're interested in it. If they go through the approval process, we're part of the determination, you know, we help make that determination, or at least we set the standard for the generation of the data that either supports the dose or doesn't, that establishes the dose.

If they go indexing, which they very well may, for those that aren't for food animals, they'll present all the information they've got on what the dose ought to be to a panel of experts, which will be experts in our opinion as well as theirs, and we always have the, we have the authority to disagree with them if we want to. It's just like most of our Advisory Committee recommendations at the agency on the approval side all the time, we have the authority to, but we rarely disagree with them.

RT: I think in some background information that you provided us, you spoke to, well, you've spoken to one of those issues already, the scientific versus social factors in resolving policy, but you also spoke about some team approach decision-making and so on. Is that anything that you'd like to mention here?

AJB: Yeah. In terms of the history of the Center, there definitely was a time in the Center, when I first came in in '72, when it wasn't clear to the folks, certainly at the review level, that it was really a part of the mission of the organization to facilitate the approval of products. I think the sense was generally, the only way that you could screw up -- and I think to some extent the France Kelsey example unintentionally fostered this -- if you could keep a product off the market, you could be a

hero. On the other hand, if you had the opportunity, as she did, to keep a product off the market and didn't, you could be the biggest goat in the history of the agency. So the only way you could really, really, really screw up and ruin your career was to say yes when you should have said no. And so it fostered a very conservative attitude, particularly with respect to food-animal products.

When Dr. Sundloff came in, he said, "You guys have got to start thinking seriously about or rethinking seriously that position. You're not considering the fact that when you deny people out there access to a safe and effective drug -- not absolutely safe but safe within reason -- they're not going to stand there and watch those animals die, food animals or otherwise. They are going to use whatever they can use to save those animals, about which we may know nothing in terms of the safety and effectiveness. That creates a bigger hazard for the animals and for the people that consume those animals than us approving a potentially marginally imperfect approval. There may be some safety hazard in there we didn't anticipate, couldn't reasonably anticipate, but that product is better than whatever they're going to use as an alternative, on which we have no information whatsoever."

That made a huge difference. It was okay to work with sponsors, to be flexible enough where it was scientifically appropriate to be flexible, to get some of these products that hadn't gotten approved in the past, to get them on the market. It took a -- not everyone was immediately receptive to that position. It took some time.

And the other thing that Dr. Sundloff did about the time he came in was he said, "This organization is not functioning as effectively as it could," and he called in some folks that worked with the Federal Executive Institute out in Charlottesville -- they're actually instructors there -- and Dr. Sundloff had gone through that whole course as far as the training up for the Center Director position. And Dr. John Pickering was one of those people who's an instructor down there, and he had a program developed which he generally, I mean, he sort of referred to as the high-performing-organization structure, and he brought those folks into the Center and we started working on that whole process, and it took a long time.

He said before he went back to the most basic elements of what it means to be a regulatory organization, what are your goals really? What is it you're supposed to be doing? And that sort of became important, to define the purpose of the organization, not as preventing anything that might in

any way be unsafe, but as finding ways to get safe and effective products, appropriately safe and effective products, out there on the market in a timely fashion. And then you start organizing and structuring your organization and funding your organization along those lines [unclear]. And he did a terrific job of turning our organization into an organization that functioned largely on the basis of team decision-making.

He wanted to find out what was wrong with the process. You don't mandate a change in the process before you go talk to the people that are actually performing the process and ask them what's working, what's not working, how could we do this better. So you started to get this ground-up approach to decision-making. And there are some new steps there, and there are people that think that that means that every decision the Center makes, everybody in the Center gets to participate in it, and that's obviously not practically possible.

But to the extent possible, using a representative situation, I mean, almost all the decisions in the Center are made by a team of people, the Center management team.

RT: I think you mentioned in a talk you gave to some folks over there once, the element of staff itself creating difficult or complicating decision-making, and maybe that's

what you're touching toward now. Is that something a little different than what you've been thinking of?

AJB: I'm not sure where you're headed exactly with that one.

RT: Yeah, I don't know. Maybe that's not . . . But you did mention also, you had participated in some kind of a grid training, and you thought that was a helpful endeavor.

AJB: Yeah. That was . . . It's interesting. The managerial grid training, I think everybody in the Center - - and this was during Van Houweling's tenure, so it was fairly soon after I got to the Center. It operated on many of the same principles that the HPO model did, the John Pickering model did. It didn't call it that then.

But one of the things that that system demonstrated to me conclusively was that in most people -- I think this is still true -- most people go through high school and college, and it's an individual pursuit, it's not a team pursuit. One doesn't study calculus as a team, one does it as an individual. And the grades that one gets are your grades. They're not some team's grades. You are judged by your individual performance through that whole process, and that's what -- I came out with pretty high marks and I was

pretty satisfied with myself as an intelligent person and a decision-maker and so on.

And so I go off to this thing, and they had this set up so that they say, "Here, let's all of us individually take this test," and you get a score, and it's a pretty good score. I go, "Hah." I feel pretty good about myself.

"Okay. Now let's take the same test as a team." This is seven people that have never seen each other before. They come from all walks of life. And they say, "You guys have to, through a decision-making process, which essentially you establish, you guys come up with some way to make a decision as a team with respect to each one of these questions that you just answered as an individual. And you've got to decide whether the team answer is better than your individual answer in any particular case. And you've got to decide whether you're going to accede to the team position or you're going to try to maintain your own position. But ultimately, the team has to make a team decision. And we will compare the results of the team decision to your individual decisions, and we will see which is better." And the team beat every individual.

SJ: Absolutely.

AJB: Every individual.

And what was most fascinating was, as fascinating, was not just that the team did better collectively than any individual could do alone, but that you learned more about the functioning of the team and the individual members of the team trying to figure out what the right answer was as a team. That was probably as important as getting the answer, the higher score, in the final analysis, was. By the time you went through that process, you know everybody on that team better than most of the people you worked with for years back at the job site. And that, to me, was astonishing, that seven people could become as cohesive using that team decision-making process in just a week than most people were in the organization you came from and had been working in that organization for a couple years. So what's clear is that the whole organization ought to start doing business that way as far as I was concerned.

And I had, in the course of my career at FDA, I probably had an opportunity to be on a handful of teams that have actually functioned as well as that team did for that one-week period, just seven strangers coming together. Here's people that are supposed to all come into this trying to do the same thing. Their mission is supposed to be very closely aligned with it. They were hired in the first place because that's what they were interested in,

and you couldn't get most of those teams to function as effectively as that team of strangers because they weren't trying hard to develop as a team, and that's what Steve brought to the Center, the ability to recognize that team decision-making was that important. I'd already had my own exposure and I was there, so . . .

SJ: Did he really change the culture, you think, over time?

AJB: He changed it significantly.

SJ: He was there forever, so, by regulatory standards.

AJB: Yeah. He changed it significantly.

I'm a little concerned because we're hiring a lot of new people, and if you don't keep at that, you know, people don't naturally function that way. It takes work, and people get busy and management gets busy, and they're focused on a lot of other things.

We had one person in the Center who's now working for Steve as a consultant at CFSAN, and his sole job was to make sure we stayed on task with respect to developing that. And we had a significant meeting every week, three hours a week, for almost, that management team, where all we worked on was that kind of, that stuff, that process, to make sure we were making progress on that process.

RT: So as you look, as a consultant now, do you see things any differently than you did when you were full-time?

AJB: Philosophically, in principle, I don't think my vision, my perception hasn't changed that much.

What's a little frustrating is that I used to think, you know, when I was a manager and had some positional authority in CVM, that I didn't exercise that authority much, that the substance and the clarity and the eloquence of my arguments were always sufficient that people just went, "Of course, that's the right answer!"

Well, it turns out that was not the case, that in fact people were acceding a lot more often, not because of the merit of my argument, but because I was an Office Director or a Deputy Center Director or an Associate Director or somebody that had some authority in the Center, because I make the same arguments now -- and I think I make them as well as I used to make them -- and people just go, they just ignore me, and that's frustrating because I think the argument should be as persuasive now, just on its own merits, as it was then, and it isn't. So, that tells you something, and it should tell every leader something about decision-making.

SJ: [unclear] influencing it.

AJB: Exactly. It's very difficult to determine to what extent the final team decision is being influenced by your position. That's one of the things that HPO says. The leader of the group takes off his hat as the leader when he comes in the room, does not sit at the head of the table; he sits in the middle of the table with everybody else. There is no leader when that decision is being made, and it turns out it's easier to say that than it is for people to act as if that were the case. And that's been eye-opening.

And I guess, from my perspective before I left, I probably had a somewhat higher opinion of the progress that the Center had made in terms of changing its culture than I have looking at it from the point of view of where I am, because some of what I thought was progress in terms of people just collegially making decisions was more people . . .

SJ: Dropping off [unclear].

AJB: Yeah, just . . . And people, even when I thought that was the way decisions were being made then, it turns out maybe it wasn't. It wasn't so much that we were all in agreement. It was, the, well, he's the Deputy Center Director, so it would behoove me to agree with him.

RT: Doctor, do you have any other areas you'd like to explore, or we've much covered?

SJ: Well, from my perspective, we've covered it, and more, but I was starting from a rather low level of knowledge, so, I mean, what you've said here has just really set the record straight in key areas, I think.

RT: Well, you've added a number of dimensions of information that we didn't have about the Center, and we appreciate very much your participating in the history program.

SJ: And if we have any more questions or you have some other things you think of that we can include, it can all be added in the editing process.

RT: Sure.

AJB: Okay. That would be fine.

SJ: Because most of the time we find that these interviews stimulate both sides to some additional thinking, so . . .

AJB: Yeah, that might be right.

RT: Quite open to that.

AJB: Okay, good. That's great.

RT: Okay. Well, thank you for now very much, Doctor.

AJB: Any idea when? When should I start looking for

. . .

END OF INTERVIEW