



Oral History Interview with
Alan Rulis, Ph.D.
Assistant to the Director for Special Projects
Center for Food Safety and Applied Nutrition
1977 - 2006

FDA Oral History Program
Final Edited Transcript
August 14, 2008

Table of Contents

| | |
|---|---|
| Table of Contents | 2 |
| Oral History Abstract | 3 |
| Keywords | 3 |
| Citation Instructions | 3 |
| Interviewer Biography | 4 |
| FDA Oral History Program Mission Statement..... | 4 |
| Statement on Editing Practices | 4 |
| Index | 5 |
| Interview Transcript..... | 7 |



Oral History Abstract

Alan Rulis is a widely recognized expert on food safety and toxicology related to food additives. He joined FDA in 1977 as a Consumer Safety Officer in the Division of Food and Color Additives, and later served as the Director of the Office of Food Additive Safety (1995-2004), and as Senior Advisor for Special Projects to the Director of the Center for Food Safety and Applied Nutrition (2004-2006). His oral history recounts the agency’s involvement in various food additive safety concerns, particularly regarding toxicological analysis of artificial sweeteners, fats and color additives and the determination of margin of safety thresholds.

Keywords

food additives; color additives; artificial sweeteners; GRAS; margin of safety; threshold of regulation; Constituents Policy

Citation Instructions

This interview should be cited as follows:

“Alan Rulis Oral History Interview,” History Office, U.S. Food and Drug Administration, Department of Health and Human Services, August 14, 2008.

Interviewer Biography

Suzanne Junod, Ph.D. is an historian in the FDA History Office at the U.S. Food and Drug Administration. Soon after beginning her career at FDA in 1984, Suzanne helped to organize the FDA History Office. She is a subject matter expert in FDA history and her scholarly writings have been published in *the Food, Drug, and Cosmetic Law Journal*, the *Journal of Federal History*, and the *Journal of the History of Medicine and Allied Sciences*, as well as edited compilations. She is an active officer in the Society for History in the Federal Government. She earned her Ph.D. at Emory University in Atlanta, where she studied under James Harvey Young.

FDA Oral History Program Mission Statement

The principal goal of FDA's OHP is to supplement the textual record of the Agency's history to create a multi-dimensional record of the Agency's actions, policies, challenges, successes, and workplace culture. The OHP exists to preserve institutional memory, to facilitate scholarly and journalistic research, and to promote public awareness of the history of the FDA. Interview transcripts are made available for public research via the FDA website, and transcripts as well as audio recordings of the interviews are deposited in the archives of the National Library of Medicine. The collection includes interviews with former FDA employees, as well as members of industry, the academy and the legal and health professions with expertise in the history of food, drug and cosmetic law, policy, commerce and culture. These oral histories offer valuable first-person perspectives on the Agency's work and culture, and contribute otherwise undocumented information to the historical record.

Statement on Editing Practices

It is the policy of the FDA Oral History Program to edit transcripts as little as possible, to ensure that they reflect the interviewee's comments as accurately as possible. Minimal editing is employed to clarify mis-starts, mistakenly conveyed inaccurate information, archaic language, and insufficiently explained subject matter. FDA historians edit interview transcripts for copy and content errors. The interviewee is given the opportunity to review the transcript and suggest revisions to clarify or expand on interview comment, as well as to protect their privacy, sensitive investigative techniques, confidential agency information, or trade secrets.

Index

- aflatoxin, 47
- Ames, Bruce, 43
- analytical chemistry, 42
 - chromatography, 39, 40
 - mass spectrometry, 39
- AOAC blue book, 21
- artificial sweeteners, 64
 - Acesulfame-K (Sunette), 66
 - aspartame, 64, 65
 - risk assessment, 65
 - sorbitol, 72
 - sucralose (Splenda), 65, 66
- Association of Official Analytical Chemists (AOAC), 21
- Blumenthal, Herbert, 13, 20
- Board of Inquiry (BOI), 64
- Booz Allen study, 59
- Brackett, Robert (Bob), 85
- Brown, Thomas, 10
- buildings
 - fragmentation of Agency functions, 58
 - North Building (Cohen Building), 12, 56
 - South Building, 57
 - Vermont Avenue, 58
- caloric value posting
 - restaurant menus, 82
- Calorie Control Council, 24
- Calories Count* (obesity report), 80, 81
- carcinogen (human), 27
- carcinogen potency, 43, 44
 - risk assessment, 45
- career
 - consumer safety officer, Division of Food and Color Additives, 8, 13, 16
 - Director, Division of Food and Color Additives, 54
 - FDA training, 15
 - University of Toronto, 8, 11
 - University of Waterloo, 8
- Center for Science in the Public Interest, 73, 74, 82
- Color Additive Amendments, 38
- color additives
 - D&C Green No. 5, 37, 62
 - D&C Green No. 6, 62
 - Red No. 2, 38
- Constituents Policy, 35, 37, 54, 62
 - Advance Notice of Proposed Rulemaking, 36
- consumer safety officer (CSO), 31
- Copp, Catherine, 71
- Crawford, Anne, 80, 83
- cyclamate, 24
- Cyclic Review of Food Additives, 9
- Delaney Clause, 19, 24, 27, 30, 35, 36, 62
- dietary supplements
 - health claims, 80
- education, 7
 - doctorate, 8
- Federal Register*, FDA publications, 31
- Flamm, W. Gary, 50
- food additive petition review process, 60
- food additives
 - artificial sweeteners, 61
 - chemicals, 19
 - fear of carcinogens, 29
- food contaminants
 - consumer petitions, 42
- food risk pyramid, 85
- food safety initiative, 84
- Fraser, Leslie, 79
- Gardner (Werzberger), Marcia, 36
- Gardner, Sherwin, 18
- Generally Recognized as Safe (GRAS), 9, 24, 30
- Generally Recognized as Safe (GRAS) review, 17, 18, 35
- Gold, Lois, 43
- good laboratory practices (GLP), 9
- Hayes, Arthur, 64
- Henney, Jane, 59
- Kessler, David, 69
- Kokoski, Charles, 13, 20
- Levitt, Joseph, 74, 79, 80, 84
- Livermore, Lawrence, 43
- margin of safety, 44
- McAuliffe, John, 10, 11
- McClellan, Mark, 80

microbial contamination of food, 85
 Miller, Sandy, 83, 84
 National Academy of Sciences, 30
 Nelson, Gaylord, 18
 notice-of-comment rulemaking, 25
 Office of Premarket Approval, 58, 60
 leadership, 60, 61
 Olestra, 68, 69, 70, 72, 74, 77
 black box, 75, 78
 WOW Chips, 75
 Oser, Bernard (Ben), 26
 packaging
 acrylonitrile, 38, 61, 63
 carcinogens, 38, 39
 polymeric, 61
 Pauli, George, 71
 personal history
 youth, 7
 polychlorinated byphenyls (PCB's), 46
 Procter and Gamble, 68, 69, 70, 74, 77
 public comment, 25
 Reagan, Ronald, 56
 recommended daily allowance (RDA)
 caloric intake, 80, 81
 recruitment, 23
 Redbook, 20, 22, 50
 regulatory policy, 50
 collaborative process, 32, 33
 reorganization
 Center for Food Safety and Applied
 Nutrition, 59
 risk assessment, 52
 Rodricks, Joseph, 47, 48
 Ronk, Dick, 8, 9, 10, 11, 13, 15, 23, 33, 54
 rulemaking, 51, 52
 saccharin, 24, 25, 27, 29, 30, 47
 Saccharin Study and Labeling Act, 30
 Shays, Christopher, 60
 Taylor, Michael, 49
 tetrachlorodibenzo dioxin (TCDD), 46, 47
 Threshold of Regulation (TOR), 43, 50, 51,
 54, 62
 U.S. Food and Drug Administration
 role of lawyers, 16
 role of scientists, 53
 vinyl chloride polymer (VCP), 41

Interview Transcript

SJ: This is Suzanne Junod in the FDA History Office. I'm here today with Alan Rulis to talk about the history of food additives. At the time he retired, Dr. Rulis was an Assistant to the Director of CFSAN for Special Projects. Prior to that he had been, for nine years, the Director of the Office of Food Additive Safety. We're in the Parklawn Building. It is August 14, 2008.

Dr. Rulis, why don't you just tell us a little bit about your early upbringing and how you came to be working for the Food and Drug Administration in the first place.

AR: I was born and raised in Illinois, attending public schools in the town of Rockford, Illinois, which is a medium-size town about 90 miles northwest of Chicago and just south of the Wisconsin border.

Throughout my whole childhood, I was interested in science. I loved chemistry; had a chemistry set. I used to do experiments in the basement and terrorize my parents with explosions from time to time. Had a wonderful high school chemistry teacher named Don Hicks. He allowed me and my classmates to express our interest in science in lots of creative ways, for example doing our own science experiments in the classroom's set-up lab after school. I ended up majoring in chemistry in college and thought I would go into academia and be a professor, just like some of my role models, Mr. Hicks, and several of my college professors.

When it came time to do that, as a "newly minted" Ph.D. from the University of Wisconsin, I ended up taking a postdoctoral position, and then another and then another. The job market was tight at that time.

SJ: Where did you take your postdoc?

AR: I did my first postdoc at the F. O. M. Institute for Atomic and Molecular Physics in Amsterdam, Netherlands. It was an interesting experience living overseas for a little over a year and doing research in molecular beam physics. Then I came to the University of Waterloo in Ontario, Canada, and worked with a professor there, Giacinto Scoles, who was in the same field as I had been in in the Netherlands. I also taught some chemistry courses as a postdoc in Canada. Subsequently I went on to the University of Toronto and worked with Professor John Polanyi, who is a well-known physical chemist. He received a Nobel Prize in chemistry during the 1980s.

I had always thought of myself as getting a position in academia. It turned out that, at that time – this was the time when the baby-boom generation was all out looking for jobs – and at that time there were 150 applicants for every job. And so you could come in second or third or fourth in an applicant pool, but if that was the case, you still found yourself without a job! This happened to me several times. I began to realize that it might be harder than I thought to find the job I really wanted in academia, to do research and to be a professor like I had always imagined.

One day in April of 1976, a letter came in the mail while I was working at the University of Waterloo in Canada. The letter was signed by Dick Ronk, who was, at that time, the Director of the Division of Food and Color Additives at FDA. The letter was exciting to me. It basically said, we have openings for interested scientists of all types who want to take on a challenging job at the Food and Drug Administration. It outlined the kinds of tasks that would be appropriate for an entry-level person with advanced scientific training, to be a consumer safety officer in the Division of Food and Color Additives or a chemist or a toxicologist in related divisions at FDA.

And I was sitting there at the desk in Waterloo thinking, “you know, I have this letter in hand, and I have some other ideas about how I’d like to spend my life, but I’m going to pursue this opportunity because this could really be”

SJ: It would be nice to eat and to have a family and all sorts of things.

AR: Absolutely.

SJ: Now, do you think Ronk had targeted you specifically?

AR: Well, no. How it happened was . . .

SJ: Yeah. I was going to say, how did it happen?

AR: Well, in the desperate straits I was in, I, along with many others, it seemed, had put my name on the American Chemical Society list of unemployed chemists. I was on the roster. And Dick Ronk had the ability to hire.

At that time, there were monies coming in from Congress because at that time the GRAS [generally recognized as safe] review of food ingredients was going on. That had been initiated during President Nixon’s time. That was in like 1969 or 1970. The agency planned to extend that review to include all the direct addition food and color additives, in what was called at that time the “Cyclic Review of Food Additives.” There were monies that were allocated by Congress to fund the GLP [good laboratory practices] programs of the agency, I think it was

Senator Kennedy who had pushed for this, and there were something like a \$20.5 million appropriation, which was a lot of money in the late '70s! Some of that money came to the old Bureau of Foods, which was what CFSAN was called at that time. This money was to be used to hire new employees, for this Cyclic Review and it was a big deal. They went out looking for new FDAers.

The first thing they did was to go to – well, one of the things they did was they went to the American Chemical Society roster of unemployed chemists. This was a smart move, because they were thinking, “let’s find people who are maybe “frustrated academics,” people who could be potentially helpful to the FDA in all sorts of academic disciplines, but who may not be in the job market right now with permanent jobs. Let’s take advantage of the opportunity.

SJ: Or fully employed.

AR: Right. Let’s take advantage of the opportunity and hire some of these people and train them. We’ll get them right off the street, and they’ll be fresh, new employees we can train for this challenging job. That’s what they did. Dick Ronk sent his branch chiefs – Tom Brown and John McAuliffe among them – off to the various places to look, and one of them was the ACS roster. They came up with the names of candidates and sent out a bunch of recruiting letters. I was the recipient of one of these letters. It was just a really nice letter and the thought of working at the FDA got me all excited, so I decided to answer it.

As is typical in the federal government, just within a couple of weeks of that time, there was a hiring freeze. In typical federal government fashion, the word went out: “Stop all hiring.” So I was really excited about getting in the job pipeline, but got this note in the mail saying,

oops, sorry, the hiring window has now closed, for how long, we don't know, but you're on ice, sorry.

Well, at that time I had no other choices. I had to feed the family and I had a child, and another was one on the way, and this was not a time to be playing cavalierly with my employment situation.

So I went off to do essentially another postdoc. I took a position at the University of Toronto, which was also an assistant professor part-time position. I taught chemistry at the University of Toronto, but also had the opportunity to work in the laboratory of John Polanyi. He was well known in chemistry at that time in his career. He is the son of the philosopher, Michael Polanyi. John was, in his own right, a successful chemist on the Canadian and world scene. So I thought, this is a great opportunity for the moment; I'll work for him.

Well, not long after I got to Toronto, in November of that year, a telegram arrived from FDA. We had already transplanted our home to Toronto; we'd moved, we were in another city, and this telegram arrived. It had been beaten up; it was tattered. My wife said over the phone that it looked like it really had been through the mill getting to us. It had been sort of stepped on and torn, and it was really kind of messed up; it must have gone through a lot of trouble to get to me. Well, it finally ended up at our door in Toronto, and when she opened it, and it said, "FDA is hiring again. Respond by 5 p.m." on the date she had opened it. "Respond by 5 p.m. because our hiring window has now opened, but only temporarily. Do you really want this job?" And so she called me at work, and I said, "Absolutely, yes. Call them back and tell them I'm interested." So, she did. It wasn't long after that that FDA said they could offer me the position.

They did need to do an interview, however, and because I was, up in Canada. The person who was going to do the interviews was John McAuliffe, one of Dick Ronk's branch chiefs. He

was authorized to travel around the U.S. and meet and interview prospective FDA'ers; he was not authorized to travel internationally. Therefore, I had to drive down to Buffalo, New York, and cross into the U.S., and sit in the Buffalo airport and wait for John McAuliffe to interview me. He finally showed up, and we had lunch together and had what felt like a terrific interview. Shortly thereafter, I was formally offered a position at FDA.

We packed and moved to Washington for what we thought might be maybe three to five years, but we had no idea what it would be like. It was a real sort of stab in the dark because this sounded like a wonderful, exciting opportunity, but who knows if it really will be; let's just go. It was a real job, which was nice. So we arrived in Washington to house hunt in April of 1977, one of Washington's best months of course, driving down from snowy Ontario. We moved in in June, we started in June of '77. We were still there after 29 years, almost exactly 29 years. So it's a very happen-stance kind of thing, one of these serendipity things.

SJ: Serendipitous, yeah.

AR: Yes.

SJ: When you came into the division, how was it structured?

AR: Well, it was quite interesting. The day I arrived for the fingerprinting and taking the oath, it was at Federal Building #8, 200 C Street, S.W. in Washington, D.C. I showed up there and did the processing, and John Fullerton and Pat Price were in the administrative office. They saw to it that I was taken across the street to the North Building, which is where the old Division of

Food Color and Additives was located at that time. The building is a big old, hulking cement construct on 300 Independence Avenue, a Depression-era building. And it had super-reinforced concrete floors, we found out later, because the Social Security Administration had initially intended to be there, and the floors were super-reinforced to hold their heavy card readers and processing equipment that was going to be needed by the Social Security Administration in the late '30s, early '40s. And so it was this monstrous building, and we occupied one whole end of the third floor overlooking Independence Avenue. Dick Ronk had the corner office that looked out over the Mall. You could see the National Gallery of Art out the windows. I mean, this was really prime space. Ronk's office shared some of that space with reviewer toxicologists from the Office of Toxicological Sciences under Herb Blumenthal. Charlie Kokoski was the Division Director, and there were others like Kris Misra, the packaging expert, and Hy Giddes a color additives expert, and Marvin Bleiberg. There were also reviewer chemists in John Howard's old Office of Physical Sciences, in his then-Division of Chemistry and Physics. These included many whose names I can't recall, including Bob Livingston, Garnett Higginbotham, John Modderman, a chemistry reviewer and FDA's expert on the Codex Committee on Food Additives, as well as another "old-timer" whose name I cannot remember now, but who was a great source of information on chemistry review.

So they took me over there for processing, and I met the people in my new Division of Food and Color Additives (DFCA), which was in the Bureau of Foods' Office of Compliance (under Taylor Quinn) at that time. The division was small. There seemed to be only a handful of people there that day, and all told I would guess less than a dozen people running, really running the Division of Food and Color Additives, including "old timers" like Hamilton Parran, Walt Schaffer, Pete Chichillo and John McAuliffe as well as the mid-level up-and-comers, folks

like Gerald McCowin, Corbin Miles, Gene Coleman, Dick Ronk himself, and my first supervisor, Tom Brown.

The agency had allocated to DFCA part recipient of an appropriation from Congress (under the Good Laboratory Practices (GLP) banner; some \$20.5 M) And they had this money from Congress to go out and hire. And, boy, did they ever hire. They brought in – I can't remember exactly how many, but there were probably more than 30 new people coming in the door from all over to various parts of the Bureau of Foods, but mostly into DFCA, the Division of Toxicological Sciences and the Division of Chemistry and Physics, all to join in the food additive program work of the Bureau of Foods. There may have been hires destined also for the Office of Compliance under Taylor Quinn at that time as well. The Division of Food and Color Additives sat within the Office of Compliance in those days.

Many of the new employees were like me, “academics” or hopeful academics-to-be someday, but not quite there, and perhaps already academics but maybe frustrated with the “soft money” of living year-to-year based on their success with grant applications and all that you have to do to stay alive in academia. Many of the new people had the same kind of background as I had, were about the same age, say, late twenties, or early thirties, and hungry for making their mark in a new job. Lean and mean, I guess I should say.

SJ: They fought their way in.

AR: They fought their way in, yes, it was a competitive process, and they were a little bit hungry for some stability and challenges. So it was a really interesting – I call it the class of '77 because many of them came in during the years '76, '77, '78, around in there. There was a

whole cadre of us, and we were in what was, say, a division run by fewer than a dozen experienced “old-timers,” as I thought of them, people who had been there a number of years, really running the division, who had the institutional memory, they knew how the place operated and should be operated. We looked up to these experienced hands for information and knowledge about what our jobs entailed and how to perform them.

They were very helpful to us because they set up the system, and Dick Ronk, I think, was probably a prime mover in all of this. But they set up, they made it very clear that in order to do any kind of credible job in the federal government, and this may sound trite, but “process” is extremely important. You needed to establish a written record of the agency’s work, there had to be “standard operating procedures” followed, and there was a regular process that you had to learn and participate in. It wasn’t just random. The importance of that impressed a lot of us. We went on training exercises and spent a week away or a week and a half in retreat and learned the history of FDA, the basic concepts of the Federal Food, Drug, and Cosmetic Act, and the rudiments of our job. And there were, as I say, probably 20 or 30 of us new folks, at least, new people, all getting to know each other, all learning the background of what this job is all about. A major teaching at these training sessions, which has stayed with me, is that nothing of significance gets accomplished in an organization like FDA by a single individual working alone. Noteworthy accomplishments are the result of teamwork and cooperation. So, motivating a team to accomplish a challenging job is a key to an effective agency like FDA. We, our teams, were chemists, toxicologists, consumer safety officers primarily, and we were sort of divided into those three categories. And we learned to . . .

SJ: And you took a chemist.

AR: I actually, I thought I was going to come in as a chemist; I actually came in as a consumer safety officer. CSO's are either chemists or biologists of one kind or another, or toxicologists – who play more of a project manager role “If somebody comes to the FDA seeking the approval for a new food-additive use, then the consumer safety officer was the one who had responsibility to make sure that all the right questions were asked, all those questions were answered, and that the administrative record was in place to demonstrate that that all had been done according to process, and that there was a written record describing all of this, and that it would withstand legal challenge. Of course we worked with attorneys in the Office of Chief Counsel as part of our responsibilities.

SJ: Who were the attorneys you worked with during this period?

AR: Some of them included Stewart Pape, Mike Taylor, Rich Cooper, Marcia Gardner (now Wurtzburger), Catherine Copp. Mike eventually rose to an executive assistant position under Commissioner Donald Kennedy. Phil Derfler was one I got to know a little later on. I'll have to stretch a little to recall some of the other attorneys. The old memory doesn't always serve me as well as it should at this point. But there were a number that we really enjoyed working with on our food additive safety issues. I personally, and I think many others of my colleagues really, I think, found working with the agency's attorneys intellectually challenging because they were trained differently, to approach issues differently from scientists. But we needed to have that viewpoint, too, of course. They needed to make sure that what we were doing from a regulatory standpoint was well grounded in the law and could withstand challenge from all sides. To do

that requires a different way of thinking about the regulations you were writing in those days than the scientists were trained to do. So, it was a very complementary process, and one that was extremely important for the success of the organization.

SJ: What's the [inaudible] perspective? The Food Additives Amendment had been passed in '58. Now, this was when GRAS was becoming controversial.

AR: GRAS was controversial, well, it had become controversial already in the late '60s.

SJ: Sixties. That's what I was going to say. So this was really considerably after that.

AR: Yeah. And because – The so-called GRAS review was a retrospective look at the GRAS status of many food ingredients on the so-called “GRAS List” that resulted from the passage by Congress of the 1958 Food Additives Amendment to the FD&C Act. During the course of the GRAS Review it raised, it did raise some concerns about the safety of certain GRAS ingredients that were used in food. Its whole motivation originally resulted from some concerns and questions about the safety of certain ingredients that previously had been considered safe.

SJ: I mean, the early GRAS list was put in place in a somewhat haphazard way.

AR: Exactly, exactly. There had been some arbitrariness there. What FDA did in the course of going to Congress in the 1970's, well after the GRAS process had been initiated, was to say to Congress, “Here, we need more appropriated monies to support the Good Laboratory Practices

(GLP) regulations to ensure, among other things, that the tests performed by private contract laboratories, say, on the safety of a new potential food additive or other food ingredient were reliable and could be trusted. At that same time – I think at that time it was Senator Gaylord Nelson of Wisconsin, held hearings (he chaired a committee, and I’m not even sure I remember the name of the committee, on the Senate side). And he held hearings and I think – I’m trying to remember who was commissioner at that time, was Sherwin Gardner acting? I’ve got to search my memory on this. But the Acting Commissioner at that time who, just before Donald Kennedy became Commissioner in about 1976, who you may know that – a string of individuals was called up to the Hill to testify before Gaylord Nelson’s committee. He would have been an Acting Commissioner at that time.

SJ: He acted three different times.

AR: Okay. So Sherwin went up, and in the course of that testimony, he announced that FDA planned to extend the GRAS review to include all of the currently approved food and color additives; we’re going to review their safety as part of the way we’re going to spend these new funds.” And we, many of us, about 20 or 30 new employees, the “class of ‘77,” were hired under the auspices of essentially pulling off this new review of the safety of all the food additives, the so-called “cyclic review,” by extending the concept of GRAS to include food and color additives.

SJ: Now, was this also the time period in which we had new methods? In other words, there’s a reason they announced they were going to re-review them. I guess there was concerns

about it, but are we talking a period of scientifically in which we had some new methods, we were, you know, were there any advances that would make this a particularly auspicious time to revisit that?

AR: I don't think so particularly. I think it was that there was a kind of concern . . .

SJ: Just good timing.

AR: Yes. It was timing, and there was this, I think there was a kind of pervasive concern about chemicals that had been accumulating in people's minds ever since the post-World War II era, and with the advent of EPA in the '70s, the early '70s, and concerns that people have about exposure to chemicals, the GRAS review and some of the questions that it raised, there was a kind of concern in people's minds about the safety of food ingredients too. And then I think because of the concern about carcinogens and the Delaney Clause, people felt, you know, maybe we need to go back and look at these food additives that were previously approved, that had been on the books for, say, 20 or 30 years; let's see if they're still safe under the current paradigm. So that was the impetus for that.

As a practical matter, the cyclic review itself, however, actually never occurred in its totality! Much of the work was done, of course, and a lot of information was pulled together, but, as a result of it, we looked back and said, you know, in reality, these additives are really safe. In fact, they're safe by large margins of safety. So there was no need to go back and actually reapprove the uses of any of them. They were "safe in use" as a matter of law and as a matter of science. That was one of the real conclusions of the cyclic review.

But there were real important fallouts from this work, one of the most important of which was the creation of what folks in the Bureau of Foods, and now the Center for Food Safety and Applied Nutrition, call the Redbook , Originally *Toxicological Principles for the Safety Assessment of Direct Food Additives and Color Additives Used in Food* (and now *Toxicological Principles for the Safety Assessment of Food Ingredients*). That document represents the first time that the verbal-oral tradition of what is appropriate to ask a petitioner for in relation to toxicological information that is important to have in the packet before you review and approve or disapprove the use of a new food additive use. Historically that developed by word-of-mouth. It had been developed since the post-World War II era by FDA toxicologists Arnold Lehman and O. Garth Fitzhugh. We were spurred on to accomplish this by leaders in the Bureau's Office of Toxicological Sciences, namely Charlie Kokoski and his boss the Office Director, Herb Blumenthal. Both were thoughtful and articulate toxicologists. Their new hires, part of the class of '77 included Victor Morgenroth and Vasilios (Bill) Frankos with whom we teamed up to draft the original Redbook. They, along with CSO's F. Edward (Ed) Scarbrough and Karen Skinner, also from the Division of Food and Color Additives formed our close-knit group who were the core of not only the cyclic review effort but who helped give rise to the first edition of the toxicology Redbook in that day.

SJ: Well, they had put out the first guidance in the 60's and that was pretty revolutionary.

AR: It was, it was.

SJ: Up to that point we said, industry, *we* (FDA) know what *we* expect by way of scientific information, to meet our standards even though we aren't going to tell you in writing what that is.

AR: That little "blue book" of Lehman and Fitzhugh was really, I guess, the beginning.

SJ: Oh, was it a blue book?

AR: It was light blue, a little small blue book, and it was published later by the Association of Official Analytical Chemists (AOAC)

SJ: I just didn't know it was called that.

AR: Well, I called it that.

SJ: They called it the Bible.

AR: I called the blue book simply because it had a blue cover, but it was actually – the version we had back in the late '70s, when we arrived, was published by, under the auspices of the AOAC [Association of Official Analytical Chemists].

SJ: Did you ever meet Garth? I thought generation [unclear] is gone.

AR: I never did, never met him. And . . .

SJ: Nelson?

AR: No, not Nelson. And the other one I'm trying to think of, Lehman.

But at any rate, the point of the Redbook was to create a document that spoke specifically to food and color additives and said, "Here are the tests we expect to see," and then to essentially have a document that would be useful as a means of reviewing the safety of food additives under the cyclic-review idea. So the Redbook that was generated – and it turned out that that was first published in 1982 – was designed to be a vehicle to update the original written requirements for toxicological safety assessment for food additives, but also to apply some new ideas to performing a re-review of existing food-additive approvals to see that they're still safe under the light of new standards, if there were any new standards. That was the idea.

When we discovered that the additives that are already approved were pretty, were still safe as a matter of science and a matter of law, that document sort of lost its value in terms of re-review of additive safety, but it has been extremely valuable to the scientists in the agency who want to be able to tell petitioners what new information FDA needs to see and to evaluate in your petition for us to review as FDA'ers so we can make a judgment about whether it's appropriate to approve it or not. So that document is still viable.

It's being updated now on the Internet, and chapter by chapter, you know, in an electronic way. Back in those days, around '82, it was only in hardcopy. But that was one of the tangible things that came up during the course of working on the "cyclic review."

So there were all these new employees, and all learning their job and all finding their niches. Many of them became leaders of offices, directors of offices, leaders in government in various places. Not all stayed in the food area; though some did. Some left and became senior people in other departments of the government and made their mark over their careers. It was a really interesting . . .

And Dick Ronk and others who hired these people were asked over the years, how did you accomplish this with this class of '77? What was the deal here? And basically the answer was, well, we did not think that it would be necessary to go out and hire already-trained people who knew all about food science and food chemistry. We were just interested in getting the best minds we could find, and we would train them and put them, essentially turn them loose, give them all the training they needed and turn them loose, and eventually they would run the place. And it was a very future-thinking kind of approach. The dozen or so of senior people who originally were serving in this division were overwhelmed because of the amount of work coming in at that time. They were doing it very diligently. But to their credit, they really had a good idea about how to move that division into the future by hiring a cadre of new people, training them, and saying, "Here, take over. This is now your job, your future and FDA's future," and they all then, one at a time, retired, but left a legacy that has served the agency well for decades.

That kind of thinking was, you know, preparing for the future by hiring fresh minds and training them well, turning them loose, and turning over responsibilities to them in a kind of optimistic sort of open-ended way was really, think it what had to be done, and it's a lesson, I think, for any agency. So, there it was.

SJ: What were you doing? What were your early assignments [unclear]?

AR: Well, for my very first assignment – it’s almost, I chuckle sometimes when I think about it. I had held this grandiose idea about going to the university and doing research and publishing. So here was my first assignment. Basically my supervisor brought me into a room to spend half-days, mornings, essentially, going through boxes of comments that had been received by the agency in response to its proposal of April ’77 to ban saccharin. And this was a huge national to-do because saccharin at that time was the one-and-only artificial sweetener on the market, since cyclamate had already come under suspicion concerning its safety at that time too. Here was the FDA planning now to ban saccharin because there was concern about its carcinogenicity as a result of it turning up positive in rat feeding studies in Canada. The study had showed bladder tumors in rats at high doses. And the agency, even though saccharin was on the GRAS list, felt that it had to propose to ban it in part because of the lurking presence of the Delaney Clause over here governing food additives. So the agency proposed to ban it. There was a hullabaloo.

The Calorie Control Council, which represented the interests of the soft-drink industry, among others, began a campaign of newspaper advertisements that encouraged readers to “write your congressman” by clipping out the advertisement; clip out this blank form and write your congressman and tell the agency not to ban saccharin. So there were many thousands of those that came in, of course. But then there were all sorts of letters coming from people, and they were piling up, over 80,000, perhaps 85,000 comments came in.

So here we were, these new employees that had just been hired and had come in the door. We were people who were there, available to help read, review and catalog these thousands of

comments. Our supervisors said, “Let’s just put these new folks to work, and they’ll learn a great deal in the process. They’ll learn what they have to do. They’ll learn about notice-and-comment rulemaking, they’ll learn about what these comments actually say, how to keep track of and catalog comments, how to organize them, and draft responses to them for future rulemaking options, because eventually there will have to be a final rule and there would have to be – all these comments will have to be addressed, responded to. So what better way to teach new employees about the issue?” So there we sat in the room, pulling comments out of boxes reading and cataloguing them.

SJ: Did each one have to be responded to individually?

AR: No. As it turned out, we had spreadsheets, and most of them fell into the category of, well, this is a fill-in-the-blank comment, and it simply says “don’t ban saccharin,” so for those we simply put a checkmark in a box. But some of the comments were substantive. They were filed by affected industry representatives, lawyers for law firms in town, for example. They were very well thought-out, they were long and detailed, contained legal arguments, and so forth, so they had to be read *in toto* and then essentially set aside to be responded to individually.

There were some very, very interesting ones. There was a large bedsheet-sized comment that came in an envelope, and when we unwrapped it, it filled the wall; it was written in calligraphy script. Somebody had taken a paintbrush and done this beautiful calligraphy of this comment in which he told us not to ban saccharin, and there it was; very artistic!

There were many letters from parents whose children were diabetic, and they were pleading with the agency to not ban saccharin because it was the only way in which their child

would be able to remain a peer of their friends at parties and places that kids would go where they could drink soft drinks. Saccharin was a soft-drink sweetener that their kid could use. And if the government took it away, that would be a terrible thing for the child. Some of these comments were really heartfelt on the part of the parents.

It took several months to go through all the comments, categorize them.

SJ: Now, I remember – you may not know the answer to this, but I’m trying to find somebody who can answer it for me. I met Ben Oser when I first came to FDA, and he says that it was his food laboratory that – and I don’t know if they were a candidate – that did the rat studies. And he said he called, was it Kennedy at that point or Lay, I can’t remember? He called the Commissioner, or they reported it through channels. But he made it clear that it was a saccharin-cyclamate mixture.

AR: Yes.

SJ: And that that started the whole ball rolling.

AR: Right, I believe that. I know that there was some saccharin-cyclamate mixture fed in one study, but there was also saccharin alone fed.

SJ: Alone. Okay. I thought these people weren’t too smart to ban it on that one basis, so there must have been some ongoing . . .

AR: No. It was ongoing. It was a mixture, but there was also pure saccharin fed too, and that showed the bladder tumors. Of course, years later it was discovered by Professor Sam Cohen at Nebraska, that these tumors were likely being caused by physical abrasion on the inside wall of the bladder by the crystals that were forming because of the high doses of the saccharin being used in the animal feeding study. This made the bladder tumor results an anomalous finding that would have had no potential to give humans cancer because the levels that people were going to be ingesting were very much lower, so the crystals wouldn't be forming. And that's the reason that over time, the ban has been removed – Congress reversed the moratorium and then the ban.

SJ: And you don't have to label it anymore [unclear] science [unclear].

AR: Correct. The carcinogen warning label is no longer on saccharin containing foods or packets of saccharin, though it must always be on the Nutrition Facts Panel of any food label, of course.

SJ: That's good to know. I had never heard that explanation.

AR: Now, as a scientific matter and as a Delaney Clause matter, it probably still "induces cancer in man or animals."

SJ: It induces cancer in animals, right but it has been removed from the NTP list of substances "reasonably anticipated to be a human carcinogen."

AR: It still induces cancer, however, in animals. So a strict reading of the Delaney Clause would require a ban.

SJ: And we were going to ban it based on the Delaney Clause. Another thing I've heard about – and I needed to ask you about it because you would know better than anyone – what I had heard is that – and my dissertation actually deals with this – that the scientists were so appalled. It was, in essence, the Delaney Clause was a vote of no confidence in FDA or whoever's, the scientists' or anybody else's ability to make these decisions, and it was an eremite case that they didn't set a no-tolerance for. And a lot of this actually had to do with pesticides, which were taken away in '54. But I had heard that scientists had sort of uniformly tried as best they could not to ever invoke the Delaney Clause in order to show that they would have banned it under the unsafe, you know, under the other provisions of the Act.

AR: Yeah, right, sure.

SJ: [unclear] clause. But anyway, maybe you could speak to that.

AR: Well, there certainly – there were a couple lines of thought here.

One was that, yes, the FDA scientists truly felt – I think the scientists truly felt that they could make these risk-assessment and risk-management decisions, but that they have been taken away from FDA by Congress; that ability, that flexibility has been taken away from FDA by Congress. FDA scientists probably firmly believe they could make such decisions and still protect the public health.

But I think that they also understood, many of us, at least, understood that, at the time, there was a kind of chemophobia in the public about cancer and about chemicals. Many in the public perceive that “chemicals” are mysterious things that were being put in places like the environment or in food, and people had no ability to properly protect themselves.

[END OF TAPE 1, SIDE A]

AR: So, to pick up where we left off, the notion of chemophobia and concern about chemicals was rampant. And I think many FDA’ers, even though they felt that Congress had taken this flexibility away, also realized that there was a concern about cancer in the public mind, even though it might have been somewhat out of proportion to the reality of that concern. But it was still there, and people could understand how a law might be passed to protect people from cancer in a way that the Delaney Clause purported to do. So it was a little bit of understanding that as well. So, yeah, there was the Delaney Clause sitting there, and as a result, I think the agency felt that it needed to act [unclear] because of that.

SJ: And they were doing under-analysis of Delaney. They were deliberately invoking Delaney.

AR: Well, I don’t think as a legal matter they were, because saccharin was on the GRAS list and, as such, it was not a target of Delaney. But it could have been. . . So what they would have had to say, and I think what they did in the reg – and I don’t remember, but the wording of the proposal should be looked at carefully for this – but some of the effect of this is because it looks

like a carcinogen, and the Delaney Clause is sitting over here, but it looks like a carcinogen and, therefore, it, in our minds, is. That may render the food injurious to health and would fall under 402(a)(1). It would not be safe even as a GRAS ingredient.

But I think the Delaney Clause was not invoked as a legal matter, but nevertheless had an impact because it was a kind of lurking presence. It was a supportive notion that this – it may have been mentioned in the reg as a reasonable [inaudible]. But you'd have to go back and check.

So then, right after that, of course, Congress – we new hires had been going through these boxes and boxes of comments and trying to get through them and catalog all of them, and we learned an awful lot about the importance of listening to the public that we served. They had tremendously varied ideas and a lot of legitimate arguments and counterarguments. It was fascinating to see and experience firsthand.

The Congress, of course, then quickly passed the Saccharin Study and Labeling Act, which requested that the National Academy of Sciences do a complete wall-to-wall evaluation of risk-assessment procedures on saccharin in particular. It also stopped FDA from banning saccharin outright by saying, "You will not ban saccharin, as a matter of law." Congress overrode that; and also put in place the warning labels saying "This product contains saccharin," etc., and then kept updating and renewing that for many, many years thereafter. Thus saccharin fell into a kind of limbo and disappeared essentially from most major foods in which it had been found. And shortly thereafter, other sweeteners came along to replace it. But that was our introduction; that was my introduction to work at FDA. And I learned from there on, also by experience, the tasks of a consumer safety officer in that setting.

One of the most interesting for me was being thrown into meetings with industry petitioners. This was a heady (and somewhat terrifying experience), as a young government employee, to find oneself in a conference room where I was to chair the meeting. Members of the FDA team, chemists, toxicologists and environmental scientists, sitting around the table, the agency people, and in would come the petitioner with his attorney or with his scientists, and they would sit at the table and essentially talk to us about the issues in their pending petition, updating us on progress, or giving us some information, or asking questions, or asking for responses, say, about “why was it taking so long, and that we weren’t able to get to the endpoint on their petition, and so forth. There we found ourselves, across the table from somebody who was probably 20 years your senior, who was probably being paid a lot of money to be there. You’re virtually a freshman and your job is to run the meeting and be as responsive and helpful, yet decisive as well, on behalf of the government and our real bosses, the people of the United States, in that setting – a pretty heady experience for a young person to have. COS’s had to get used to doing that.

Part of the responsibility of the CSO was to managing petitions and see to it that the agency’s final action on it found its way into the *Federal Register*, if there was an approval or not, whatever the case. If there wasn’t an approval, there would have to be a denial that had to be published. As a CSO, I had a variety of experiences with direct food additives, color additives; packaging materials, which at that time were petitioned for approval. Some of what a CSO must do is to convene the team of FDAers working on a given petition and work with the scientists in our own organization to reach a conclusion. This sometimes requires working with those in the team or elsewhere in the agency who might have different views. So part of the job

is to reconcile different views and reach the ultimate conclusion of the government, i.e., the government position on a given project.

What you realize, what you learn fast if you're paying attention at all, is that you are not defined so much by your personality, or your coworkers are not defined simply by their personalities, as such, although they are – I mean, they're people, and you learn to work with each other – but that those who contribute to a conclusion about the review of any given situation, are people who occupy positions. Those are positions of responsibility, and they have duties, they have official relationship with other positions in the government. So, you have an official position; that is, in addition to being a person, of course, your personhood, you and others occupy official positions, and you have to respect that, and you have to understand that that is what really defines your job and your responsibilities relative to others. You have to execute your job in light of that position that you hold. And so it's a responsibility factor that you learn to identify with, and you learn to carry it out in a way that focuses on the government agency reaching a decision that is in the interests of the people it serves, that is consistent with the statute, that is a binary decision that basically could go either way. It may be scientifically a little bit uncertain; there may be uncertainties surrounding the decision. There will always be residual uncertainties surrounding the decision. And your job is to bring all the scientists on the team around to the issues together in such a way that finally a "binary decision" emerges that the agency can stand behind, both scientifically and legally. Even though there may be very different personalities around the table, very different scientific views around the table, ultimately the responsibility is to reach a decision that squares with the science, in the interests of the government and the consumer, and is consistent with the law, consistent with past practices and precedents of the law, on behalf of both the petitioner and the American consumer,

serving them and their interests under law... all in view of the these residual uncertainties. It's a challenging job (just as Dick Ronk described it in his initial recruiting letter) with a high level of responsibility, that you have, and that everyone on the team has.

One challenge in doing this is to allow for differences of opinion to be openly discussed and debated. Our class of '77 had to acquire these skills pretty quickly, to learn how to bring diverse people together around the table, work through a difficult problem with lots of nuances and scientific uncertainties, boil it down to a decision, figure out a way to get to the responsible and scientifically sound decision, and then to write the necessary regulation. In this environment one had to learn how not to squelch anyone's opinion arbitrarily, to not step on anyone's scientific views arbitrarily, to accept and listen to all views, and then, if necessary, to reject and override some views (on the record), and but to make this very clear in the administrative record that you were doing that consciously, with respect for that approach or that opinion, but reaching another conclusion or opinion based on the weight of all the evidence that everyone had evaluated and considered.

So it's an open process, a documented process, in which each reviewer has a right to their opinion, and then one in which one reaches, finally, a definitive conclusion that the FDA can stand on. The end product is, in fact, an administrative record that documents everything about how the agency reached a given decision on a petition or other application. That's a big order and something I don't think my formal education prepared me for. It is something one can only attain from experience on the job, with good mentors and role models. Certainly nothing in my academic career, prepared me to do this. This FDA job I had found was truly the job that was somehow advertised between the lines of that letter I got from Dick Ronk, and it was very exciting and challenging, as predicted.

SJ: It's a collaborative process.

AR: Yes. And one that you just don't describe very easily to anyone else who hasn't experienced it. But then you learn as you do it, and you look back at it and say, "Wow, that's what's happening here," what an amazing job this is. And, of course, it was and is, and what a challenge. And nothing really prepares you for that unless you actually do it.

SJ: Jump in and get wet.

AR: Yes. So, to me, that's the great revelation of the working in FDA that you work on behalf of the American people, petitioners and consumers alike, you come to these kinds of decisions that you need to make, and it's a kind of mindset and a kind of process that nothing really prepares you for unless you actually do the job itself. And few people perhaps appreciate it unless they actually do it. So in this way we learned our jobs over the years. As time went on, some of us competed for other kinds of positions and moved up the ladder and became branch chiefs and division directors and had more and more responsibility thrown at us because if we were doing anything well at all, people will sort of single us out as someone who could jump in and meet the next challenge. As people in the "class of '77" moved on, there were some more opportunities to apply for competitive positions. And so, in many of our cases, we took on more and more responsibility and found our way through the organization and along a kind of progressive pathway.

When I look back on my career in the food-additives area, the kind of highlights that pop out at me include what I just described, the whole idea of doing the job and what that involves; the challenge of the cyclic review and realizing, finally, that it wasn't going to actually end up being a process of re-doing the safety of all the food additives because when you did the job, as we did the work, we realized that, yeah, we did a lot of cataloguing and literature reviews and reevaluation of the safety of additives in a way that allowed us to conclude that, hey, these additives are all quite safe, in fact. So let's not waste effort, but let's use the benefits of what we've done here to find ways to streamline and make more effective the process that's currently in place for the new food additives. What we did, therefore, was to translate the ideas from the cyclic review back into the process that is used every day to review the safety of new food additives. So, in the end we got a lot of benefits out of it.

Then, there was the Constituents Policy, which was an interesting, challenging project in policy development. I think Rich Cooper was in the General Counsel's office at that time, if not chief counsel. Marcia Gardner (now Wertzburger) worked with us closely on delineating the options around that policy proposal. We also worked with Nancy Buck, General Counsel in that time period.

Terry Troxell was one of my close co-workers, hired the same year as I was. We worked together on the Constituents Policy. In fact, we originally roommates as "FDA freshmen" in 1977, and back when new employees were housed two to an office (an excellent way, by the way, to train new employees!). The Constituents Policy was an attempt to deal with the application of the Delaney Clause not only to additives themselves but also to any possible carcinogenic impurities or trace constituents that might be present in an additive from, say, the chemistry of its manufacture, etc., to try to keep from having the Delaney Clause be applied to

everything under the sun (and of course many new trace constituents were being discovered all the time because of the constant advances in analytical chemistry), not only things that were carcinogens themselves, but things that might contain carcinogens as unintended constituents or impurities.

What the agency had been doing at that time was saying not only would we apply Delaney to an additive that was itself a carcinogen, in keeping with the Delaney Clause, but that we would also apply it to any trace constituent or contaminant or impurity of an additive if it was found to be a carcinogen, even at a minuscule level, and even though the additive itself that contained the impurity was NOT a carcinogen! The gist of the policy was to say, Well, if “it” – the word in the Delaney Clause – If “it” is shown to cause cancer in man or animal, that “it” applies only to the additive itself, not any constituents or inherent impurities of the additive. And if you could show that the constituents of the additive, by appropriate means of risk extrapolation, would not result in anything more than a trivial level of risk, doing a quantitative risk assessment in the conventional way, then it could be present there and not banned under Delany. The use of the additive itself, along with its constituent would still be consistent with the general safety clause of the food-additives safety standard (i.e., reasonable certainty of no harm). But it would be allowed to contain that carcinogen even in spite of the Delaney Clause, which would have prohibited the additive if it had been the carcinogen itself.

Terry and I worked to develop the policy (with the help of general counsel) and put it in the *Federal Register* as an Advance Notice of Proposed Rulemaking in April of '82, I think. As I said, at that time, the Office of General Counsel . . . The person we worked with there was Marcia Gardner (nee Wertzberger). She insisted, somewhat to our annoyance – we pulled a lot of our hair out trying to deal with this, and I came to appreciate what she was doing – that we

propose a *range* of options for the ANPR, not just our preferred one. I did not appreciate what she was doing at the time, but I do appreciate it now in retrospect. She was forcing us to put several ideas out, because this was, after all, an Advance Notice of Proposed Rulemaking, and she believed that it was important for the agency to be seen opening the door to other ideas, put out other options, and go from “our wonderful option” that we thought was so great, and add other viable options and put them out there and let people shoot at them. That was one of her major contributions, and that was a very good idea.

We published that document, as I say, in '82, and, of course, it was immediately challenged in the courts in *Scott vs. FDA*. This was a case involving a color additive, namely D&C Green No. 5, I think, with the carcinogenic impurity, para-toluidine. As it turned out, the FDA won that case in court and essentially memorialized the Advance Notice of Proposed Rulemaking as that concept of the Constituents Policy in case law. It established it as a viable policy. But the strange thing was, the ANPR was never finalized, never brought to the proposal stage let alone finalized. It's been successfully invoked by FDA now for 25-plus years. And it has been challenged in court only one other time, in the case, I believe, of D&C Green No. 6 and para-Toluidine. FDA won that case as well. As a result, it has been used as a policy by the agency for all these many years, at least a quarter of a century, without ever being finalized.

SJ: Was there anything, in between that '77 and '82, were there any specific products or any specific – you said that the public was going crazy with some of this stuff. It started with saccharin, of course, and all the rat studies and whatever. But were there any others after that that were . . .

AR: We've got many carcinogens.

SJ: Drawing ire or whatever?

AR: No. Well, there were some, I think there were some visible food-additive issues that were always roiling things, and they were, oftentimes in this era they were related to colors. There's a long history of concern about colors, as you know. Red 2 had been dealt with early in the 1970's before we came on the scene pretty much. When I arrived in 1977, that had pretty well been dealt with, but the repercussions were being felt. FDA was in the throes of re-evaluating the safety of color additives that had been put on what was called the "provisional list" and for which new studies had to be conducted and reviewed and new updated judgments made about the safety of numerous color additives in use since the passage by Congress of the Color Additive Amendments of 1960. So, yes, there were a lot of concerns in peoples' minds about how the agency was dealing with these things. And cyclamate had just been deemed a safety problem in this time frame too. And so, between sweeteners and colors, one problem or crisis or another was continually coming up.

Another issue that was in the forefront at that time was packaging materials. People didn't really know how to deal with low levels of monomers and oligomers that were showing up in polymeric plastic soft-drink bottles that were being invented at the time. One of the inventions was the acrylonitrile bottle, which was a very good gas barrier and could keep the carbon dioxide in the soda bottle, keep oxygen out, the pressure high, preserve the quality of the beverage, etc. The bottle was made of acrylonitrile, a plastic polymer. And as with any such polymeric resin, there would be residual levels of acrylonitrile monomer molecules floating

around in the plastic which could never easily be totally eliminated, and which could exit the plastic and get into the food. As it turns out, acrylonitrile is known to be a pretty potent carcinogen that, in rat studies, would exhibit tumors in just about every organ system one can imagine, from brain tumors to liver and lung and everywhere else.

SJ: Not on the GRAS.

AR: Not on the GRAS list. And a target of Delaney. So one of the challenges of the late 70's in DFCA. And just as I was coming in the door in '77, there were people already at the Xerox machine preparing for the acrylonitrile hearings.

And the issue that that raised, which is one that has dogged us for years, was the presence of exceedingly low levels of chemicals that might migrate to food from food packaging materials. When we started looking with more and more sophisticated analytical chemistry techniques, one would see more and more molecules that weren't supposed to be there, undesirable entities in food-contact materials particularly, but also in direct food additives and color additives. This was perplexing because as you began to see more and more of these low levels of substances popping up in your chromatograph and mass spectrometer in your other highly sensitive analytical techniques, you would be faced with having to figure out a way to deal with them in a regulatory way. And the tail – in fact we sometimes said, “The tail's wagging the dog,” but it was even worse than that. The hairs on the end of the tail were wagging the tail that was wagging the dog. That was how bad it seemed.

SJ: Okay. This is something I really want to get a little clearer on. But when do all these new technologies for testing . . . I mean, what I hear is that we went from being able to test million parts, you know, parts per million to parts per billion.

AR: Right.

SJ: What time frame are we looking at? What equipment? [unclear] mass spectrometer?

AR: Yeah. I think that this was . . .

SJ: Well, we had mass spectrometers long before this.

AR: Sure, sure, we did. But I think that the gas chromatographs, liquid chromatographs, the mass spectrometers of the time, and sometimes putting them together in tandem and figuring out ways to couple the mass spectrometer as an analytical device with a gas or liquid chromatograph to really refine the information that's coming out of that instrument, allowed people to look for and find smaller and smaller quantities of things that shouldn't be where you didn't want them. So it was, and it was a revolution that was taking place probably starting in the '50s, with the development of better equipment, vacuum chambers, etc, even from the '50s and '60s on, but all the way through into the '70s and '80s. Every year analytical chemistry would get better and better. You could find laboratories that could look harder and find smaller amounts of things every year than the year before.

SJ: And is around when NIH set up their register, what they called the Carcinogen Register?

AR: I don't know but it's possible, yeah, and then people would for carcinogens . . .

SJ: Because they have a list.

AR: Yes.

SJ: Things to look for.

AR: Right, yeah, and then people could look. One of the polymers that people were concerned with was vinyl chloride. There was a . . . You know, vinyl chloride polymer was also a very effective barrier resin that could be used in packaging food, in contact with food. But vinyl chloride monomer was also a carcinogen. And when FDA's analytical chemists went into their laboratories to try to determine whether there was, how much vinyl chloride might be in a particular polymer matrix, they had to be so very careful. Some complained that if they did the measurements in a laboratory that had vinyl tile on the floor, they could see vinyl turning up in the detector as a result of its just coming off the floors. It was . . .

SJ: That's very sensitive.

AR: Yeah. So you're talking about measurements that were done and had to be done in very clean laboratory settings in order to just be sure that you were measuring only the sample you were looking at and finding those atoms that weren't supposed to be there in that sample.

So analytical chemistry is progressively getting better and better and better, and, as a result, people were turning up sighting these unwanted trace impurities and other things. And the regulators had to figure out what to do with them because they would hit the headlines of the newspaper, "compound X found in food Y," or "compound X found in packaging material Y," which can get into food Z.

So the matter-out-of-place notion, the idea that a food is "contaminated" by or could be "contaminated" by a chemical that shouldn't be there is alarming to the public no matter the actual level, it is – to anyone, it's alarming – and it's something that could ratchet up public opinion could easily do by saying, "You, as an innocent consumer, are going out and buying food assuming it's safe and pure, and look what's in it." Consumers have no control over that, because how in the world could it have gotten there, how can you get it out, and so this sort of level of concern and unease with minuscule amounts of chemicals out of place became ever-increasing.

And so one of the tasks that we had to try to face from a regulatory point of view, was, people would come to the door with petitions for packaging materials to be in contact with food. If one could go to the laboratory and start measuring, seeing small, very small amounts, minuscule amounts of monomeric materials coming out of the polymer into food, it would be necessary to go through the full-blown petition review process and to get an approval, even though those migrating levels might be so low as to produce no more than negligible risk to the

public. There might be so little migration in some cases, that you'd have a hard time saying that anybody could have a real-life risk as a result of this exposure. But there they were.

A real challenge at that time, in the '80s, was to try to figure out a way to keep the tails, the hairs on the end of the tail of the dog from wagging the dog. I mean, that was the preoccupation with these small amounts of materials. And we were seeking a way to draw up what we called a "Threshold of Regulation," policy to help us define a level of exposure below which one could say, you know, no matter what this material is, unless we happen to know it's a carcinogen, let's not worry about it because the exposure is so low. Let's find something else to spend our finite resources, the taxpayer dollars, on. And so that was the genesis of the notion of Threshold of Regulation policy, another idea from the 1980's. It was the idea that we could in fact find or determine an exposure level to materials that was probably safe per se, unless it could be shown to be a pesticide, heavy metal, or a demonstrated carcinogen. And that policy was pretty much launched by coming across accumulated data compiled by Dr. Lois Gold at UC Berkeley and Lawrence Livermore.

Dr. Gold, who had worked with Bruce Ames, was working on cataloguing potencies of carcinogens and published a wonderful compilation of them that she had in her database of so-called TD50's for hundreds of chemicals that have turned up positive in rodent bioassays.

We found in the Journal *Environmental Health Perspectives*, there was this wonderful catalog with all these potencies. So we went to our, what we now today consider to be really clunky computers, and we put all of the potencies that she had compiled, and plotted out the distribution curve. We saw that the distribution curve was Gaussian. It was a perfect bell-shaped curve when potencies were plotted logarithmically. It was a gorgeous, smooth curve. And we said, "My goodness, this is amazing. If you take these potencies, which are all kinds of

chemicals fed to either rats or mice, and when you plot the distribution of their potencies in this specific way, they form a beautiful bell curve. What a gift! It's not just random. There's a bell curve. If you have a bell curve, you can draw a vertical line down the middle of it or off to one side and block off some area of it and say, "You know, if I restrict my attention to one part of this curve or another, I can discount or ignore the other part in a quantitatively reliable way. So let's figure out a way to use this curve's shape. It's so well behaved. All the carcinogens that have ever been found in rodent feeding studies, all the chemicals that have ever been found to be carcinogens fall within this nice bell-shaped curve. Why can't we use the shape of it to help us formulate a policy?"

So that was the genesis of the threshold-regulation policy. With that notion, we were able to come up with an exposure level to any noncarcinogenic chemical likely to present no more than trivial risk, even if it turned out, unbeknownst to us later to be a carcinogen. The exposure level we arrived at turned out to be a half a part per billion in the diet. This was pretty arbitrary, but it makes good sense in light of the data. It was an exposure level such that the preponderance of noncarcinogenic chemicals would be excluded from presenting anything more than negligible risk of carcinogenesis, even if they later turned out to be carcinogens. That's how that policy came about.

SJ: Well, now, that kind of replaced the hundredfold margin of safety or . . .

AR: Not really – no. The hundredfold margin of safety is a tried-and-true methodology that comes out of the Arnold Lehman and O. Garth Fitzhugh era. Anyway, the safety assessment paradigm of looking for a highest no-effect level and applying a safety factor of a hundred to

account for the genetic variability of humans and to account for the extrapolation between animals and humans is a tried-and-true methodology that's still applied today, and that is in place and still works.

But what this was, was to say, let's, for special situations where there are noncarcinogens involved, but where we want to assure that if we do not subject such a situation to premarket regulation, that even if the substance we're exempting turns out to be a carcinogen, the risk is not likely to exceed one-in-a-million. For this we use a linear proportional extrapolation from the known levels of risk observed in laboratory animals to zero dose, zero risk using a straight line down to zero risk – zero dose. This very crude linear proportional extrapolation says we will accept the fact that there might be some non-zero risk from a carcinogen at some low, unspecified non-zero dose. Whatever the dose is, there's going to be some risk. So that's, let's draw that straight line from the dose at which we know risk has been demonstrated in animals down to zero-zero, and then use that line as a means of extrapolating to some small level of risk for a correspondingly small level of exposure; and then, looking at the bell-shaped curve, say, well, if we try to exclude most carcinogens or potential carcinogens from being anything more than, let's say, an upper bound of one-in-a-million lifetime risk of getting cancer, what would the exposure have to be, if you were extrapolating down that straight-line curve? And the answer turned out to be a half a part per billion in the diet. A half a part per billion in the diet will prevent well more than half of those carcinogens in the bell-shaped curve from ever producing anything more than a one-in-a-million upper-bound lifetime population risk. So why not just pick it as a reasonable place to be on that curve? We could have chosen to be even more conservative by prevented *anything* under that curve from providing anything more than a one-in-a-million risk, but then the policy would have been essentially very difficult to use in the real

world, because if you're going to prevent all risk from all potential carcinogens, even those as potent as TCDD [dioxin], which is a million-fold more potent than most average carcinogens, then you have no policy. You essentially decide to spend all your resources to eliminate the last picogram of the most potent material you can imagine. That's not a useful policy.

SJ: Where would you find that? I've never heard of that.

AR: TCDD? Well, it was tested and shown to be extremely potent, actually in trout, but also in rodents too. Some very, very low levels were able to cause cancer.

SJ: What is it, and where do you find it?

AR: Tetrachlorodibenzo dioxin. It's a . . .

SJ: Say that slowly for our poor transcriptionist.

AR: Well, it has a long chemical name. It's 2-3-7-8-tetrachloro-dibenzo-para-dioxin, I think, more or less [note to SJ: listed as 2-3-7-8-tetrachlorodibenzo-*p*-dioxin at NIH website]. It's a compound that is actually fairly commonly found in some industrial settings given that its cousins, polychlorinated byphenyls (PCB's) used to be used as an insulator in electrical transformers and things like that. And it turns out . . . Dioxin is a compound that is has a history of use as a defoliant. It is a component of Agent Orange, you know, that was used during the Vietnam War to clear jungle growth; Anyway, it is a very potent carcinogen. And if you try to

protect everyone from all risk from carcinogens, but assume they're all as potent as TCDD , you'll basically have to take the gross national product of the country and devote it to avoiding the last picogram, you know, a part per million million or so, of that material. So those kinds of assumptions just rule out any public policy or risk-assessment, any risk-management decisions.

[END OF TAPE 1, SIDE B]

AR: Well, so, let's see, where were we?

SJ: Well, I wanted to talk a little bit about aflatoxin.

AR: Yeah. I don't have a lot of specifics on aflatoxin, but I might be able to recall a bit about my interactions with Joe Rodricks. Aflatoxin is, among other things, known to be a potent carcinogen. It is off on the high-potency end, the tail, of that carcinogen potency bell curve we talked about. It is not quite as potent as TCDD, but still potent.

SJ: And you said saccharin was at the other end.

AR: Saccharin is totally the other end. It's one of the least-potent carcinogens that you could imagine. And if you believe the results of the animal feeding study to be relevant to humans, which we now know it's not at normal levels of dietary intake, but if you just take the results of the animal feeding study, that's where it ends up.

I was fortunate to interact with Joe Rodricks in CFSAN (Bureau of Foods) in the '80s because when he was a higher-level advisor to the Bureau of Foods Director and practiced risk assessment and toxicology on behalf of the director at the time. Very quickly thereafter went up to work with, I think, Donald Kennedy during Dr. Kennedy's last months as Commissioner. It could also have been Commissioner Hayes, Arthur Hull Hayes, I can't remember. Or, even our Commissioner from the University of San Francisco, Jere Goyan.

SJ: Jere Goyan.

AR: Jere Goyan, yeah.

SJ: It's Kennedy, Goyan, Hayes.

AR: It could have been Goyan, it could have been Hayes, it could have been both. So when I was still a "freshman" FDAer, Rodricks had gone up to the Commissioner's office and was advising on risk assessment matters across the agency. He was one of the leaders, and still is, of course, in doing risk assessment on chemicals, looking at their dose responses in feeding studies and understanding something about relating that information to possible or potential human risk scenarios, and dealing with the uncertainties in that.

SJ: And knowing that that's not perfect.

AR: That's right.

SJ: But we can take what knowledge we have and extrapolate.

AR: You can sometimes only learn something about extreme situations and say the risk is probably not more than a certain amount. These are things that Joe is very good at doing, and I think he was good at explaining to the Commissioner and other policy makers. He has always had a remarkable skill at doing that.

SJ: Talk about Mike Taylor a little bit.

AR: Mike was an attorney in the Office of General Counsel. I met him when he had been assigned to work on some food issues. He attended the University of Virginia, and graduated from the University of Virginia Law School, and came to the agency and was a star pretty early on. I do remember encountering both Mike Taylor and Joe Rodricks, as well as Stuart Pape while working on some of these policy problems that I've just been describing. When briefing the Commissioner and the Commissioner's staff about them, they were involved in those briefings.

Mike also was involved in our discussions on Constituents Policy and development of the options there. And also, at one point, during his tenure at FDA he was involved in encouraging us to reform the GRAS petition process. Mike was very encouraging to us in the foods Center to tackle that problem. It was very reassuring to us to know that he supported the redesign of that program. It spurred us on immensely.

So, all of those gentlemen were really very effective FDA'ers both inside the FDA, when they were here, and also outside the FDA in their private-sector careers afterwards, and still are. I'm also reminded of W. Gary Flamm, who among other positions was a Director of the office of Toxicological Sciences for a time. Gary was a mentor and guiding light in the creation of the Redbook minimum testing levels.

Okay, so threshold regulation. One thing I want to say about Threshold of Regulation policy development, even Constituents Policy development for that matter, that is so remarkable to me, looking back on it now, is that today, in the federal government, agencies like FDA and other science-based agencies that want to develop policies to deal with issues, have enormously more constraints on them than they did in the past. We were able, in those days, to think of solutions to these kinds of problems, develop them, brief our superiors, give talks, publish papers, and promulgate new policies, brief the Center Director and the Office Directors at the time, and eventually move up the chain, drafting regulations in conjunction with attorneys in the Office of General Counsel, put policies in the form of a proposal, say, and get them out for comment with very little second-guessing from the Office of Management and Budget. This is not true today. There are downsides and benefits from the way it works today, but for sure in those days, it was a lot easier to put a new approach on the street. We were able to engage in the notice and comment rulemaking process in a much more unencumbered way. It still had its checks and balances, which was extremely important to have, but it wasn't so encumbered that it couldn't be done at all.

I think that what you find today is that rulemaking has to go through so many levels of internal control and external control and peer review that it's virtually impossible to accomplish unless it is mandated by new statutory language. So the government . . . And I can see the

rationale for it, because you don't want haphazard rulemaking and you don't want arbitrary rulemaking. You don't want the regulatory agencies to promulgate rules that are unnecessarily restrictive and that don't benefit the public health enough to warrant the costs of those regulations. So the Office of Management and Budget has a legitimate role to play in being a gatekeeper.

But often what I see now, in looking at it in retrospect, is that today I think really good science-based regulation is oftentimes a lot harder to promulgate today because you have many more people involved in the decisions about whether to go forward and under what rules you will go forward in making these kinds of proposals. Back in the day when we did TOR, it was very, we were, it seemed, very much freer to come up with ideas, put them on paper, get people to buy off on them, and promulgate those at least advance notices, if not notices of rulemaking, and then get them memorialized and actually working.

SJ: I was under the impression at least that a lot of this OMB came with the, increased scrutiny came with the Reagan administration.

AR: Yeah. Well, perhaps, the thought was to exercise more control of the regulatory agencies so they don't get "out of control," kind of thing. And I can see both sides of the issue; there are two edges to that sword. You could also argue that regulation, that if someone did not want a regulation to hit the street, if the OMB is insisting on peer-reviewed science, then arbitrary, people who want to stop a regulation from hitting the streets because they're using bad science would also have a burden, that if the OMB is insisting on peer review to assure that the science

used in making a rule is appropriate, then people who are using inappropriate science to stop a rule would also have a burden. So it is a two-edged sword.

SJ: Right. Well, I just learned that apparently – I didn't know this, although probably I should have – for any regulation, you have to have basically the value of a person-year or value of a person. It made the news that the EPA had just lowered the value of a person. And, of course, it's a statistical thing. It's not really that. But I do want to do a little bit of digging, a little bit of the history of that, because it seems that different agencies value it differently, I guess, for the purposes of rulemaking. But, to me, it's just fascinating.

AR: It is interesting. In fact, I acquired over the years a file, and referred to it often, that was a compilation of some articles written by authorities in the field, talking about risk decisions and risk management under uncertainty and in view of competing risks, acceptance of risk by the public and risk management. Often the topic focuses basically on how much risk is being mitigated by a particular rule, and at what cost? And there are compilations of, you know, your chances of having certain things happen to you, being struck by lightning, for example, or being killed in a car accident, and what it costs are to avoid those events or prevent them. There are many compilations such as these that have hit the pulp, and lay literature, but also in the scientific literature, to show that the government regulatory agencies that have responsibility for public health and safety have sometimes promulgated rules that have cost the public a lot of money while mitigating very little risk. But then some rules that have not been very expensive at all have prevented a lot of risk. So there needs to be a kind of leveling to this. And I think one of the, at least the higher purposes of OMB, at least ostensibly, or on paper, is to provide a basis

upon which a rational judgment is made about how much risk is being avoided and at what cost, and to do that in a way that's in the interests of the nation as a whole.

SJ: And that extends across government agencies.

AR: Right.

SJ: Especially among agencies that have tons of money and those who have less money.

AR: Exactly. And so that while the different decisions are being made across the federal government with taxpayers' dollars in relation to this risk mitigation. So, to me, it does make some sense.

But I think also that with an agency like the Food and Drug Administration, it is a science-based agency, and scientists work in it and those scientists have the opportunity to develop policies and respond to problems. And if you don't trust those scientists to do their best work, and you hobble them from, you know, you make it impossible for them to ply their trade and to make their best judgments, you dissuade the best scientists from entering the agency to work. That's a risk.

You do need to have an opportunity for scientists, if they want to be in a world-class scientific organization, then they do need to be given latitude to do their best work and to publish and be given credit for that work. If you second-guess the science and subject it to unnecessary political oversight to stifle it, you run the risk of losing the best scientists, and then you'll have a less effective scientifically based organization, so there's a concern with that.

SJ: Okay. Let's anchor it back in your career. So, during the '80s, you were working – well, give us some guideposts to hang things on.

AR: Yeah. What happened was the Constituents Policy or threshold regulation had sort of gotten started in the '80s. One of them was published, became effective as the Advance Notice of Proposed Rulemaking for Constituents. Threshold of Regulation sort of took a slow track between 1985, when we began to define the beautiful bell-shaped curve and figure out how to get a policy made, and we published some papers. We went to conferences and talked about it. Industry saw it as a potentially good thing because it provided a floor below which these analytical methodologies we talked about before would not be a problem.

So there was an incentive to promulgate a rule, but it took until about 1995 or so to actually publish a threshold-regulation policy in the *Federal Register* and incorporate it in the *Code of Federal Regulations*. So it took almost a decade. And in the meantime, I had become the director of the Division of Food and Color Additives, and then found my work and my world changed because, in that kind of a position, you don't have the opportunity to sit back and think creatively about solving scientific or policy problems anymore. You have a daily grind of many, many things falling upon your desk that have to be addressed at any given moment.

SJ: So you were basically the successor of Dick Ronk.

AR: Yes.

SJ: Okay. Directly, or through somebody else?

AR: Jerry McCowan had been the director of that division before me while Fred Shank was director of the Center for Food Safety and Applied Nutrition. I was unsure about whether I really wanted to do this “director thing,” because I knew that it was going to take great effort, and would require me to take time away from my family, to focus on the challenges of the job, so I had mixed feelings about it, but decided to go ahead and do it, so that was that.

I started as Division Director in November of 1990, so that sort of ended the ‘80s into the 1990’s timeframe. Then things began to be much more varied because my job was now very multidimensional. I had responsibility to manage a larger organization now, with all the personnel issues that come along with that. Also, the kinds of issues that come before you in that position are the ones that don’t get solved below you, and so you end up spending your time working on the hard things or the intractable things, and it’s a very demanding but challenging position.

And in the course of all that, just after I was selected as Division Director, a decision was made by CFSAN director Fred Shank to move the Division physically across town to Vermont Avenue NW.

SJ: Any weird motive for that, or just needed space?

AR: Yeah. Well, what was interesting – this is a story that I don’t know whether or how much interest there might be in this. But, as I said, when we first came, when I first came to FDA, we were occupying offices – the Division of Food and Color Additives was occupying offices in the

old HEW North Building; now it's called the HHS Cohen Building. We were there because the division at that time had no laboratory contingent. We were office-bound scientists, chemists, toxicologists, CSO's who worked at desks. They did not have a laboratory to work in. So they could be moved into various office spaces wherever it became available.

Since 1977 we had been occupying this beautiful office space overlooking the Mall, as I had mentioned, and it wasn't long after Ronald Reagan was elected President that Mr. Reagan came to visit that very building. He didn't come to visit the regulatory agency, of course. He came to visit the Voice of America down the hall and also throughout the building. The VOA occupied a large part of that building as well, on the second and third floors, primarily. And it was a big deal when Reagan came for his visit because – I'm trying to remember. I really am not sure I can tell you for sure whether the Hinkley assassination attempt had already occurred, but I think it had, because security was really tight. There were decoy convoys coming and going with sirens blaring and agents planted on all the street corners. And they didn't bring the president in via the front door; they brought him in his limo down the loading dock into the basement of the building and then through the corridors of the basement in the North Building, which I'm sure if you know anything about, the way they are constructed, it's a labyrinth of basement corridors with steam pipes and all sorts of hand trucks and people working.

Anyway, they took him in through that route, and then up the escalator, elevators and escalators into the Voice of America offices. I think he even made a broadcast from there. During his visit to the building the security detail kept us FDAers sequestered on our end of the hallway. We were not Voice of America people. They put guards out in the corridor and said, "You will not move about while the President is in the building," and they kept us sequestered off on one end of the building.

Well, it was just a couple of weeks or so after his visit to that building, we were informed that we FDAers (DFCA, and the toxicologists, chemists and everybody from FDA there on the third floor) were told that we were being ejected from the building, that the . . .we had to find alternate space.

SJ: Do you think he had something to do with that?

AR: No. It was that the Voice of America needed more space and... He'd visited there. And I suspect that somebody may have said, "By the way, if you can do anything about getting us the rest of that third floor corridor, please." And so we were just told to pack out; we had to find other space. And they moved us to the South Building, right across C Street, and so we had . . .

SJ: South Ag?

AR: No, South HHS at 300 C St.

SJ: Oh, okay.

AR: South HHS. And so it was 300 C Street instead of 300 Independence Avenue. So we were moved off the Mall and lost our prime space overlooking the Mall and the Capitol Building, of course. But the North Building had its charm, because on the third floor, you did have a view of the National Gallery, the domed National Gallery, and the rest of the Mall looking slightly northwest.

But we ended up being in the South HHS building for a number of years. And then, eventually, Dr. Shank moved us in December of 1991, over to Vermont Avenue after I had taken over as Director of the Division. Not long after that, in November of 1992, the Center was reorganized along product lines and the Office of Premarket Approval was created out of primarily the three divisions I mentioned earlier, the CSO's from the DFCA in the old Office of Compliance, chemists from the old Office of Physical Sciences, and toxicologists from the old Office of Toxicological Sciences.

SJ: But you're still out in the middle of, sort of out in the middle of nowhere.

AR: Yeah, strange thing that we were . . .

SJ: Strange place.

AR: Yeah. We were . . . But we actually got to like the space because it turned out it was some of the nicest federally rented office space in the District of Columbia area. It had been previously rented by the Cosmetics, Toiletry and Fragrance Association, including some of their attorneys, I believe, so the place was pretty nice. It still looked better than any federal government office space that any of us had ever seen, so we enjoyed it immensely, of course. . . . Anyway, so, yeah, so we were there from 1990 on.

I mention real estate a lot (our original location in the North Building, then the South HHS building, then Vermont Avenue and after about 2003, the Harvey W. Wiley Building in College Park, Maryland), because office physical location was a very pervasive reality for all of

us at FDA at that time. Aside from the Commissioner's office in Rockville, MD, FDA was split up into 30 or 40 different locations around the DC area. We in the food additives area were in 3 or 4 of these locations over those years, and it made a tremendous impact on our efficiency. Remember, this was in the years largely before the advent of efficient electronic communications. People were just getting used to e-mails and setting meetings up electronically, and conference calls. Being split up in several buildings had a huge (mostly negative) impact on productivity (though sometimes we were glad not to have certain senior people just down the hall from us, so to speak). A lot of time was wasted crossing town to attend meetings; a lot of efficiency lost. In the first couple years of the 1990's Dr. Jane Henney was Deputy Commissioner for Operations under Commissioner Kessler.

SJ: Under Kessler.

AR: She later came back to be Commissioner from 1999 to 2001. Anyway, at that time, then, in about November 1992, there was a big reorganization of CFSAN. Dr. Henney was at the helm of that. She'd brought in people from Booz Allen to assist. And one of the goals of the reorganization was to CFSAN from being a program oriented management system (such that it was organized around scientific disciplines) into a product based organization with Offices devoted to FDA regulated product categories such as Seafood, Plant and dairy foods, Nutrition and Labeling, Food Additives, etc. Prior to that there had been, as I mentioned, an Office of Toxicology, an Office of Chemistry and Physics, an Office of Compliance, and so forth, Office of Nutrition and Food Sciences. What the reorganization under Dr. Henney did was to cut it the other way and make an Office of Food Additive Safety (it was originally called the Office of

Premarket Approval) among others. In fact, my original roommate from 1997, Dr. Terry Troxell eventually was to become the director of the new Office of Plant and Dairy Foods and Beverages

And so they reorganized CFSAN and created the Office of Premarket Approval, which would bring together toxicologists, chemists, and CSO's, who all had worked under different scientific offices and could never be brought together in a coordinated way to get the job done efficiently, all were brought together in one office. I was selected as head of that office by Dr. Shank, the Center Director. So we had been given the opportunity at that time and in that setting, to kind of redesign and rework the food additive petition review process to make it much more efficient and get people working together as a team or set up priorities across the office that would involve everybody that needed to be in a team to report to the same bosses, that had the same performance expectations, and that allowed us to become much more efficient in operating. And that was my challenge. We reengineered the process. We basically designed it and made it work.

So a lot of my focus during those years was management, and how to create effective leadership, and how to do "leadership" as something different from "management." It was management in the bureaucratic sense, but it was leadership in the motivational sense. The challenge for me at the time was how to become a competent and good leader, how to be an effective leader of a major office in a key regulatory agency with scientists involved in that job, and to do so even on a shrinking budget, because throughout that whole period of the '80s and early '90s, the budget got smaller and smaller, and the possibilities for doing things with the money became less and less viable. And then it was . . .

So we were, back in the '90s, we were actually . . . The industry finally got fed up with the slowness of the process, and we were called up by Congressman Shays, who headed the

subcommittee of the government operations on the House side, maybe in June of 1995, so five years after, that I became Division Director. Five years after that, a hearing was held, and I testified about the process of food-additive rules and procedures. It was after that that the Center and created an Office of Premarket Approval and reengineered the food-additive approval process.

The main challenge of leadership for me at that time was to get an organization of very smart, very effective people working together with one set of goals. As a result I focused much less on science as such and a lot more on the challenge of organizing people to get behind a set of priorities in order to get a job done.

SJ: Any particular issues that came to the forefront during that period?

AR: Yes, indeed there were. There seemed to be a stream of new sweeteners coming before us at that time. Also there were issues relating to substances (sometimes carcinogenic monomers) migrating into food from polymeric food contact materials, like plastic soda bottles.

SJ: You didn't tell me.

AR: Well, just prior to when I arrived at FDA in 1977 many (especially new hires) in the new and growing DFCA were busy preparing for a hearing on the acrylonitrile soda bottle. This was during the tenure of Commissioner Donald Kennedy, in his era. Also at that time the agency was trying to deal with vinyl chloride polymeric resins too, and the migrating carcinogenic monomeric vinyl chloride. What resulted from dealing with these issues, ultimately, both the

“Constituents Policy” and the Threshold of Regulation policy. The Constituents Policy we developed and published as an advanced notice of proposed rulemaking in April of 1982 and the TOR policy in 1995, almost 20 years later!

The issue, that the Constituents Policy attempted to solve was that prior to its implementation, the agency believed it was obligated to ban any (noncarcinogenic) additive under the Delaney Clause if it was known to contain a carcinogenic impurity that might also become a component of food, at however low a level. The Constituents Policy clarified that the agency believes the word “it” in the Delaney Clause, “if IT is shown to induce cancer in man or animal...” pertains to the additive itself, but not to any constituents or unintended impurities (such as reaction products, monomers, oligomers, etc. that might also be components of the additive, even if they are known to be carcinogens in animals or man. Rather, the policy said, the risk presented from these impurities should be assessed quantitatively by using risk assessment techniques (namely linear proportional risk extrapolation from animal laboratory data) to arrive at a dose that is associated with an upper-bound lifetime risk of cancer for humans that does not exceed one in a million. In this way, the policy said, the risk presented by the constituent or impurity can be shown to be negligibly small and consistent with the general safety standard for food additives of “reasonable certainty of no harm.”

Thus, the Constituents Policy was a terrific new approach and partial solution to handling such problems. It was immediately applied (in the same issue of the Federal Register as its publication (April 2, 1982) to the case of D&C Green No. 6, a color additive that is not a carcinogen, but which contains the carcinogenic impurity para-toluidine. That application of the policy was immediately tested in the courts (*Scott v FDA*) and the agency prevailed. Within a couple years, I believe, it was tested again in *Scott v FDA* in relation to D&C Green No. 5 and

para-toluidine. Again the agency won. This set an important precedent upon which the agency has built its continued and repeated application of the Constituents Policy thereafter and into the present (even though the original ANPR was never published as a proposal or finalized, but was rather retracted for “housekeeping” purposes in 2000!)

SJ: Bottles [inaudible] marketed.

AR: The acrylonitrile bottles failed in the marketplace, I think, because probably the cost was too high to produce them and there were more profitable bottles coming out made from cheaper materials, including PET (polyethylene terephthalate, the ones you see today in most soft-drink aisles of the grocery store. Actually, I think there may be some acrylonitrile bottles still around in some offices somewhere in the agency. I’m sure somebody has one. In fact, there’s – someplace in this agency, there’s an acrylonitrile Coke bottle with actual Coca-Cola in it sitting somewhere. I remember seeing it years ago! It’s probably in CFSAN somewhere.

SJ: Well, I don’t think anybody would let me know.

AR: You should ask around because I’m sure that . . .

SJ: If they’d just let me photograph it, that would be fun.

AR: Yes indeed. And then, of course, during the '80s and '90s, we had our, you know, there was a string of sweeteners, sucralose, ace-Sulfame-K, continuing controversies surrounding aspartame, aspartame's variant, neotame, stevia, etc.

SJ: Well, say something about them because that's the thing that everybody's interested in.

AR: Aspartame has, for whatever reason, has been a lasting source of controversy for the agency dating back into the 70's.

SJ: Now, I understand there were some serious problems with aspartame.

AR: Well, as I say, aspartame issues go back into the '70s. It was one of the very first issues I dealt with when I started at the agency. At that time the agency was preparing to hold a Board of Inquiry to look into the safety of aspartame. (The original regulation had been stayed.) The Board, overseen by an administrative law judge is one means the Commissioner has of adjudicating an issue of controversy. Advisory committees are another. BOI's are a seldom used process here at the agency. It's in the regs, Part 10 of the regs. It allows you the agency to convene a group under an ALJ to investigate primarily scientific issues. The aspartame BOI occurred under Commissioner Arthur Hull Hayes.

I wasn't directly involved in the process, but had some responsibilities to gather and organize information that was to be reviewed by the board. Once the board came back with its recommendation (not supportive of the safety of aspartame) Commissioner Hayes overruled the Board in his final conclusions and determined it to be safe for consumption by the general

public. This left aspartame on the market as a safe sweetener. And so it's controversial to this day. Still most scientists at the agency today are convinced that aspartame is safe for use. There had always been people who had felt strongly that aspartame was unsafe for a number of reasons, but the scientific information refutes these concerns. It's repeatedly been shown to be safe in use and safe as a matter of science, and it still is safe as a matter of law today. And even today the controversy persists. There were recently studies from the Ramazzini Institute in Italy that purport to demonstrate carcinogenic effects from aspartame ingestion by test animals. These have been discounted by agency scientists, who have noted that these studies do not conform to the usual protocols for such studies. Not only that, but the FDA scientists had difficulty in getting access to the pathology slides to evaluate. This conclusion has been mirrored by FDA's counterparts the new European Food Safety Authority EFSA headquartered in Parma, Italy.

One of the advantages we have today, as opposed to the 1970's when saccharin was the only sugar substitute available, is that with a range of such sweeteners there are alternatives, and any possible concern or risk, if there is any, is spread among many additives. Aspartame doesn't survive high temperatures and therefore it cannot be used in baking. This is not true of the sweeteners acesulfame-K and sucralose. Sucralose is now called Splenda. That's the popular or trade name of the sweetener. And it's had its own somewhat interesting history.

[END OF TAPE 2, SIDE A]

AR: Sucralose is a molecule that is, to start with, a sucrose backbone. Sucrose is a double-ring structure of glucose and fructose hooked together – that's sucrose, common table sugar. Then chlorine atoms are attached, covalently, three chlorine atoms, two on one ring and one on

the other ring, so that you have trichlorogalactose sucrose, which is a molecule that has the sweet properties, this very intense sweet flavor on the tongue (about 300 times sweeter than sucrose itself), but is noncaloric. Because of the shape and size of the molecule, it is not able to be metabolized and therefore it just passes on through your body and is excreted. So a detectable effect is felt on the tongue, and that's it.

We at FDA, during our review of the sucralose petition had a few rocky moments. We discovered, way too late in the process, I think, that there was an unresolved issue that had to do with the test animals in some studies showing a more-than expected body-weight-gain decrement while on sucralose dosing. This effect was not easy to explain, and the resolution of it took months and delayed final action on the petition to the consternation of the petitioner and to us at FDA as well until it was resolved. FDAers fought for the conduct of new studies to resolve the issue and won that fight. The company did the required studies to FDA's satisfaction and so ultimately the additive was approved after all the data were consistent with the safety standard of reasonable certainty of no harm.

The data we looked at was extensive, and we concluded on the basis of our review that sucralose is safe in use and therefore approved it. And it has been – those approvals were extended to include all food, not just nonalcoholic beverages, but all potential food uses with good manufacturing practice as the only stipulation. The maximum amount used is limited by the taste factor. With the approval of sucralose there was one more additional high intensity, sugar substitute, on the market. It is also capable of withstanding baking temperatures as well, unlike aspartame.

Acesulfame-K is another one that was approved in the '80s, with extended uses permitted in the 90's to include nonalcoholic beverages.

SJ: Brand name?

AR: Sunette; Sunette is one brand name. There might be others out there. It's in soft drinks and various sweetener mixes with other sweeteners.

So, unlike the day when we were freshmen here in 1977 and there was only one sweetener on the market, saccharin, and we had to ban it, there now are a number of safe alternative intense sweeteners (sugar substitutes) for use in soft drinks and for other uses, such as baking, etc.

SJ: I started using Splenda in baking.

AR: It's a wonderful alternative.

SJ: My family doesn't know the difference.

AR: Well, my mother, who's now 95, going on 96, is type-2 diabetic, and she is thankful that there are alternative sweeteners like sucralose-sweetened cookies that she can enjoy without having to worry about sugar affecting her blood sugar.

SJ: That's right.

AR: So we had – a lot of those issues were popping up all through my tenure as Director of the Office of Food Additive Safety. Olestra was another major . . .

SJ: Now, talk about Olestra.

AR: Olestra – that was a P&G project that was originally a goal of P&G scientists for use as a cholesterol lowering drug, actually. As a food ingredient, it was seen as a potential replacement, ultimately in the food area, a replacement for fats, frying oils. But they had, I think, some, originally some drug uses in mind for cholesterol-lowering. But it eventually came to the old Bureau of Foods as a fat replacer, a molecule that has physically the properties of a cooking oil. It is different from actual triglyceride fat, however, in that it is nondigestible by the GI tract. The molecule it's made with starts out a lot like the one we talked about, sucralose, a molecule that is based on sucrose. Instead of attaching chlorine to the sucrose double ring structure, one attaches 5, 6, 7, or 8 chains of big fatty acids hanging off of it. It then has the property, unlike sucralose, which is a crystalline material, has the property, depending on the number and length of fatty acids attached, of a liquid, like cooking oil that can withstand high temperatures and so therefore is able to be used as a frying agent, a deep-frying agent, or a fat in baking. Upon ingestion, it is not able to be attacked by digestive enzymes in the human stomach, so that it passes right on through. As a food ingredient, however, it provides the oiliness of the fat and the opportunity to bake and fry things, fry foods, but because it is not digested, does this without providing calories.

So the joke went, among FDAer reviewers, between the two additives sucralose and Olestra, you have the “holy grail of artificial food ingredients” they produce a sweet taste and

oily mouth feel of a luxurious fried or baked food without any calories! This was during the time when nutrition advice was directed primarily at reducing fat in the diet as a means of weight control. Procter and Gamble had their petition for Olestra before CFSAN for years. As Commissioner Kessler remarked in the course of review in his final decision on the approval of Olestra, “We reviewed 12 shopping carts full of data of all types related to toxicology and physiology and GI tolerance, and nutritional safety issues to reach our decision on Olestra.”

Reaching that decision was complicated. Olestra is a boring molecule from a toxicological standpoint. It doesn't do anything. It's not absorbed significantly or digested by test animals anymore than by humans. When it gets into the gut, nothing much happens. It goes in one end and out the other. In the course of that transit, none of its bonds gets broken or metabolized. Where there is no chemical or metabolic breakdown, there is no opportunity for toxicity in the animal studies or in humans, and so, frankly, it was seen from a toxicological point of view as rather uninteresting.

The problem that did arise, however, was that it behaves like a fat both physically and physiologically in the GI tract, so it had the potential to absorb and sequester within itself fat-soluble vitamins. Such nutrients can partition into the Olestra in the gut and be swept out of the digestive system before being absorbed by the body! That had the potential to lower your plasma levels of vitamins A, E, D, and K, the fat-soluble vitamins. If those vitamins were part of the food you were eating, they might get sequestered into and end up in the olestra and be excreted rather than absorbed by the body for use as a nutrient. You could in principle, therefore suffer reduced blood plasma levels of these vitamins over time, if you eat enough Olestra. So for FDA this was a nutritional issue that related to safety that had nothing to do with toxicology per

se, but that had to be evaluated by CFSAN scientists who had to be sure that the olestra met the safety standard of reasonable certainty of no harm from that perspective.

SJ: So you had to work with the nutrition side of this.

AR: Yes. And we had to design studies for P&G to do that would allow us to understand how much Olestra caused what levels of Olestra in the diet could decrease plasma levels of the fat-soluble vitamins, and how the adverse effects of that could be avoided. One question was could you add those vitamins back to the foods that olestra was being used in, so that the sequestration of those vitamins into the olestra fraction would not cause a depletion of them from the body's blood plasma levels.

SJ: They were already desaturated.

AR: Yes. The idea was to place within the Olestra containing food, just enough of the vitamins you're worried about (A, E, D and K) so that the net result is that those vitamins that are part of the food you eat are not depleted and your blood levels don't drop. We were able to design studies for P&G to do that they then executed in pigs to provide the necessary data for our reviewers to review. Pigs were chosen because of the similarity of the pig GI tract to that of humans. These were full-grown test animals fed olestra in these nutrition studies. The studies were able to give us the necessary quantitative understanding of how much vitamin add-back was necessary to prevent depletion.

SJ: The strategy of adding it back did work.

AR: Yes, it did. As a condition of approval, then, in order to be safe in use, the Olestra had to... Any food that olestra was going to be used in had to have those vitamins added to it. But they weren't actually "enriching" the food with those vitamins, however. Therefore we had to figure out a way to tell consumers on the label that these vitamins had been added, because they had to be on the label, but they weren't doing anything other than preventing these vitamins from being depleted upon digestion. Now, how do you explain that in 10 words or less on a label?

SJ: [unclear], yes.

AR: So this was a big challenge that our teams worked on. George Pauli the Office's senior policy advisor (and member of the class of '77) was instrumental, along with Catherine Copp, who was an Office of General Counsel attorney, worked on it and did a wonderful job of working with our people, Linda Thorsheim among others and George Pauli and others, to devise the regulation that would allow for the safe use of Olestra under these very stringent conditions, with certain labeling restrictions.

Another "interesting" aspect of Olestra was that it is not digested but is excreted through the GI tract. Thus, it did have the potential for causing some GI discomfort. If there is bulk in the gut because it is not digested and it is being excreted, there is the potential for some cramping, potentially, or other discomforts, or even loose stools (not diarrhea. And I say "not diarrhea" because what we discovered in the process of looking at the data is that patients in

clinical trials weren't having diarrhea as such—including water loss, as happens in clinical diarrhea, with the flu, say) but simply softer stools

We spent much time looking at nutrition studies involving humans where we tried to find out whether there, you know, what levels of intake would give rise to what levels of discomfort (say, cramps, loose stools or other physiological effects) and try to deal with the question of whether that type of effect was a safety issue or not; whether, if someone experienced a feeling of discomfort in their lower GI, did that make the use of Olestra unsafe for any reason? And if not, did the consumer of that food still deserve to know that that might happen since Olestra was something new and different in food, and that they might have discomfort in the low bowel. A person would know that might happen to them if they ate prunes or drank a lot of apple juice for example, but they would probably be surprised if it happened to them after eating a bag of potato chips that were made with Olestra. So you had to address the issue of how do you inform people about this potential for discomfort if they ate a lot of olestra containing foods, say a large amount of potato chips made with Olestra?

SJ: Well, there was an example. We did that with a sweetener, too. I can't remember the name of it. It's an artificial sweetener that we used in candies and things.

AR: Yes, sorbitol or other sugar alcohols.

SJ: Sorbitol, right.

AR: The same kind of thing happens. You get osmotic diarrhea there, in the lower bowel, and you may have very loose stools as a result of eating lots of these sugar alcohols

SJ: Yeah. My son found that out the hard way.

AR: If you eat certain sugar-free candies or some things like that, it can happen.

SJ: I think he got into some. I don't remember. Because I wouldn't have given it to him directly necessarily.

AR: Right.

SJ: It wasn't amusing at all, but it was amusing in the sense that it taught him not to just grab something.

AR: Olestra was a challenge because it was difficult to explain clearly all these nuances in our final rule document. It became a rather lengthy *Federal Register* document. All of these issues had to be laid out in significant detail.

There was opposition to our approval of Olestra by the Center for Science in the Public Interest. Mike Jacobson opposed our approval of Olestra and hated the idea of it being on the market. He even hired blimps to fly over football stadiums at half-time, advertising that people should dial a certain phone number if they have had a problem with Olestra. I mean, it was a real public relations campaign going on against Olestra. And there were, of course, spikes in the

number of people who reported adverse effects directly attributable to these press events, i.e., coinciding with publicity that would appear in newspapers. So a question arose as to what was the truth and what was imagined here.

One of the stipulations in the approval was that in 30 months the petitioner, that is, P&G, had to come together with the agency and join us in a public hearing before the FDA Food Advisory Committee, and also including the Center for Science in the Public Interest and any other interested members of the public, to participate in the review of whether or not this new food additive that we'd approved was still considered safe after having had 30 months of experience with it on the market.

We held an advisory committee as well before FDA made its final decision to approve olestra. We had a four-day session in which we brought in gastroenterologists, pediatric gastroenterologists, nutritionists, toxicologists, and scientists of all types, corporate people, corporate representatives. P&G presented, of course, and so did the Center for Science in the Public Interest people, and other interested consumer advocates. And we allowed everyone to present for four days. We talked about toxicology, we talked about fat-soluble vitamins, we talked about drug interactions, we talked about gastrointestinal effects of olestra, and the entire transcript of that hearing, the verbatim transcript, is part of the record. And, as I said, we repeated the process 30 months afterward too. We had approved Olestra in '96.

SJ: Ninety-six.

AR: January of '96, we approved Olestra, and 30 months after the approval, we had the second Advisory Committee meeting, and that was three days' in duration. Joe Levitt had just

become the Center Director at that time, so that was his re-initiation into the food genre for him, too. It was a three-day marathon of discussions about everything we ever knew about Olestra's use in light of now having had 30 months of experience, and the conclusion was basically the same, that it was safe when we approved it, and it continued to be safe. But that did not quell the objections to its use by those opposed to it, and there was a lot of publicity again and a lot of disagreement in the public media about it. There were many, many cartoons and op-ed pieces and discussion points published about it, both pro and con in the lay literature and the scientific literature too.

SJ: But I think all of us are aware of the potato chips. Was it Yes or O or something?

AR: Well, the original – Frito Lay had some test marketing names for the original Olestra chips, but they ended up with WOW chips.

And there's been some issues about the label statement. One of the stipulations for the approval was that there be a box on the package that was separate from the nutrition-facts panel that said, "This product contains Olestra. Olestra may cause abdominal cramping and loose stools. Olestra inhibits absorption of some vitamins and other nutrients. It also said, "Vitamins A, E, D, and K have been added." However, it didn't explain why. (It was, of course, to compensate for any possible sequestration and loss of these vitamins from the GI tract due to the olestra.) And this was all put in a black box, so people conceived of it as a warning label and it was talked about as a "warning label" in the popular media. Technically, it was not a warning label; it was an information statement for people to know that when they looked at that consumer-facts panel and they saw these A, E, D, and K vitamins having been added to the

olestra containing food, they would know why. They were added to compensate for any depletion of them due to olestra.

SJ: The loss of those, yeah.

AR: There was nothing nutritionally – these foods therefore weren't being fortified in any way for nutrition purposes; the vitamins are added to prevent net loss or depletion of these vitamins from the body. As for discomfort, if you are one of those people who ate a lot of the Olestra chips, say, and you have experienced cramps or loose stools, the label box was there to help explain that this may be a reason. It was there to let you know that, if abdominal discomfort was happening to you, you should consider cutting back on your intake of this product. That's all. But there was nothing about that that was unsafe as such, however, you know, as a matter of health protection.

SJ: Would olestra ever become popular as, for example, for fried foods and things, did it have a different mouth feel or something?

AR: Yeah, it did. It had a waxier mouth feel to some consumers.

SJ: Yeah, because otherwise Kentucky Fried Chicken, you know . . .

AR: Right.

SJ: . . . would have been [unclear].

AR: One of the initial intentions of Procter and Gamble when they came forward with their petition was to have it be approved not only for savory snacks in bags, but for French fries in fast-food restaurants and in Kentucky Fried Chicken, probably, and even in bottles in your own kitchen shelf so you could then fry your own food in it. And when we did the exposure assessments and looked at nutritional concerns and the gastrointestinal side effects, potentially, that could result from these huge, potentially huge exposures from these other uses, we said, “That will just not work. You must restrict the list of foods you want to put it in and the applications you have in mind.” So we made much narrower the group of foods that would be allowed for using olestra as an additive.

SJ: Oh. So that was a regulatory, not a marketing decision.

AR: Yes. It was a regulatory decision. And then, of course, when it finally was approved, I think people – I don’t think it was that big a seller. Frito-Lay had contracted with P&G to use Olestra as a fat frying agent in their “WOW” chips. WOW Chips was the name.

SJ: Wow, that’s it.

AR: Yeah. And I don’t think that name really took off, and part of it was, I suppose, the adverse publicity, but part of it was maybe a flavor factor, who knows, mouth-feel factor. But

Olestra chips are still on the market as far as I know but under another name. But they're more of a niche market.

SJ: And that's essentially the only product there is.

AR: Yeah. It's because the regulation sequesters it off into savory snack foods.

SJ: Oh, so it's in snack only.

AR: The regulation is very narrow. Now, I think there still is a petition pending, or there was a petition pending, for microwave popcorn. I couldn't tell you the status of that.

SJ: That's a snack food...

AR: Yeah, but it was not a savory snack; it was excluded from the initial approval, so there was a question about whether they could use it in microwave popcorn. And then there was a subsequent rulemaking during my tenure that involved the label, removing the requirements of that box, that black box, and essentially saying, well, people now know pretty much that this is what it's going to do, so the label box statement was deemed no longer necessary.

SJ: Yeah. I've been trying to do a little history of the black box, and we think of it as being a drug thing now, but it actually started as a food thing in the '30s.

AR: Oh, interesting.

SJ: They required – there was a big debate over whether you were going to have branded foods or graded foods, especially in agriculture. Peas, for example. You took Le Sueur, get them to market, they are tiny peas under their brand so that people knew what they were getting. Or did we just establish agricultural standards, grade A, grade B, grade C? Well, this was during the Depression, of course. It made sense to look at the grade labeling. And so what they did basically was, they went with grade labeling, but they had a substandard grade that they put in a black box: This product is below standard but good food, basically. I think that was what [unclear], but of good nutritional value, whatever. So that's the first use I found of it. [unclear].

Anyway, did you have anything else you wanted to say? The new leadership, for example?

AR: Well, I will just mention two things. One of the things that Joe Levitt did when he came to CFSAN was he saw the importance of leadership for CFSAN's future and set up a leadership training program and asked me head up an effort to make that happen. I was asked to chair a Leadership steering committee and task force. That was a difficult assignment. But we eventually launched a leadership training program. This was ultimately taken over and brought to maturity by Leslie Fraser, at that time relatively new senior hire in the center, who was very effective in making leadership training a reality for CFSAN. Since then it's still in effect today, and I think it's a very good one. So that was one of the things that I focused on in my last [unclear] time with FDA.

And the other things I got involved in when Joe Levitt was on board as Center Director were nutrition issues related to obesity, and dietary supplement health claims. And we did two reports for Commissioner McClellan. One was a task force report that dealt with qualified health claims for dietary supplements and conventional foods, and the other was the obesity report, *Calories Count*, that addressed issues relating to what FDA's role in obesity prevention. That role focuses a lot on FDA's responsibilities with the food label.

For both of those two task forces and doing those two reports, and I was responsible for pulling together the writing teams for those two projects and bringing those reports to fruition and rolled out publicly. In this work I was so pleased to have the support and organizational skills of my assistant, Anne Crawford. She had come to CFSAN on a detail from the agency's executive operations staff and stayed. I was able to have her work with me, pretty much as my executive assistant for my last couple of years at FDA. She was very organized and energetic, and made those reports possible. We were pleased for the second report, the *Calories Count* report, to see a photo of the Secretary of HHS, Tommy Thompson, holding up the agency's *Calories Count* report on the front page of the *Washington Post*, above the fold, when it was released. We felt was a real accomplishment for FDA.

SJ: Was there any discussion at the time of creating... Well, the reason this comes up is, you know, Michael Phelps is winning medals right and left at the Olympics, and there was an article in the papers, maybe the *Post* or somebody, anyway, basically saying that the poor man consumes – poor man – that the man consumes 12,500 calories a day, which was, what, three times, nine times what's proposed under the generous allowance for males that age. So, was

there ever any discussion about adapting the food label in some way to account for short people like me or athletes...

AR: Basically...

SJ: You would never get to the athletes' point. But it seems to me like that generic 2,000 calories a day is just that.

AR: It is. It's not...

SJ: It's not so much the nutritional label is not helpful. It is; it tells you calories and portions, very much so. But that that number may be really off for the highly sedentary population.

AR: And there is some accommodation to that because the number on the label does give different caloric intakes for men and women, I think, very appropriately. But it is, you're right, 2000 calories per day is a crude figure that is not a customized figure for every individual based on either gender or body size or body mass index, and so it's something that's very personal and something you need to kind of know for yourself what the appropriate number of calories is for you on a daily basis.

But in the *Calories Count* report, the message there was it's not so much that you should have a certain number of calories a day, but that you should have that number of calories that you're going to burn, so if you ingest more than you burn, you'll gain weight, even if it's only a tiny bit more, a percent or so. More than a percent or two of calories more than you need, you'll

start to gain weight. If you eat a percent or two of calories less than you need on your daily activity basis, you'll start to lose weight. And that equation governs, is the simplest way to talk about nutrition and obesity and weight maintenance, and it's a very simple rule-of-thumb and one that is missed by a lot of people who try to come up with all sorts of fancy diets and everything else that may or may not have validity. Truly it's the calories that count, and that was the message of that report.

SJ: [unclear]. And CSPI has done a great job, I think, having been called the food police, you know, partly because of the [unclear] findings [unclear].

AR: Yes.

SJ: They've done their part in showing where hidden calories are.

AR: Oh, absolutely, particularly on restaurant foods.

[Brief break in record].

During the time of our obesity report, Ruby Tuesday was one of the few family restaurants that ventured into the realm of putting calories on their menus. As a matter of fact, on my desk, I had a Ruby Tuesday menu with calories by every item, not just the "Smart Eating" part, but the whole menu. And I think they found that it was a turn-off to their consumers, who couldn't deal with this, didn't want to be reminded how many calories they were ingesting, and so they removed the calories from the menus.

SJ: Do you still have a copy of that?

AR: Somewhere, probably you would find it – I bet the person who would have it, would be able to come up with it, is my wonderful assistant Anne Crawford. Yes, Ann Crawford, my assistant, during my last couple of years at the agency, knows about that menu and probably would be able to locate it. She would either have it somewhere in her collection or she might be able to get it from Barb Schneeman

SJ: Well, talk to me a little bit about working in the Center. You talked about Levitt a little bit. Bracket came in.

AR: Bracket was a microbiologist.

SJ: You were under him the whole time, right?

AR: No. I was under – when I first came aboard, it was, I think Howie Roberts was Acting Director of the then Bureau of Foods after Virgin Wodicka had left. He was on his way out, and then it was, Sandy Miller. Miller was hired not long after I came to FDA. Sandy Miller was Bureau (Center) director for a good part of my tenure at the FDA. I have great respect for Sandy Miller, who was a tremendous scientist.

SJ: I was going to say I remember when you first come to FDA and you start reading all this stuff on a daily basis, it does something to you, and they talk about like physicians get these diseases that they're studying.

AR: Yes.

SJ: Well, I got totally freaked out by a lot of the stuff. And Sandy Miller gave some speeches in which he says, "After all, it's okay to have a Snickers bar every once in a while," and he eats one every once in a while. And I thought, "Oh, thank . . ."

AR: Thank God. Yeah. He's a terrific guy, a real human being, and a true intellectual. You know, a lot of scientists talk a good game, but some seem to lose their ability to be amazed and interested in things. Sandy never lost that. He always retained his ability to be fascinated by science and to be amazed and be an inquirer. He could also propagate excitement about learning and discovering as a scientist. I always admired him for that.

Sandy was an MIT nutritionist.

And Fred Shank after him for several years, then Joe Levitt in 1998 with a mandate to propel the "food safety initiative" a Clinton era multi-agency, multi-department initiative to fruition. After that, was Bob Brackett.

To me, Joe Levitt was an very interesting guy to work for. I got along really well with him; we hit it off great. He had a different tack on things because he came to CFSAN as an attorney, but did a good job, I think, in many ways directing the Center. He tried to get CFSAN focused on its priorities and get everybody working in the same direction. "PPD" was a favorite

acronym of his – meaning “policy, priorities and direction”: The “big arrow” toward which everybody in the Center should be working – and he’d get everybody’s “little arrows” signifying these three elements, pointing in the direction of his “big arrow” signifying the Center’s overall PPD. He would put a big arrow down and say, “I want your arrows pointing more or less in the direction of my arrow. I set PPD; I set policy, priorities and direction for the Center. Your job is to align your work with everybody else in CFSAN to the extent possible so that it gets us all going in the same direction.”

Bob Brackett came in in 2004, I believe. Brackett was a University of Wisconsin-trained microbiologist, who had then gone to the University of Georgia. He was then hired by FDA during the era when food safety and microbiological contamination of food was still a big issue and getting bigger. He was relatively new to CFSAN when he was chosen by Commissioner McClellan to succeed Joe. Bob was a valuable asset to the Center because at that time, microbial contamination of food was the real major food safety issue faced by the agency; certainly not food-additive issues. Food additives are really safe relatively speaking, while not probably in the minds of consumers.

SJ: That’s the irony.

AR: And that’s the famous Howie Roberts perceived food risk pyramid, you know, the idea that people think that the true food safety risks come from food additives and pesticide residues and chemical contaminants, and that nutrition is not anything to be worried about, and microbiological contamination isn’t either, because concern about it disappeared at the turn of the century, the last century before this one, around the early 1900’s. And it’s actually the other

way round. Microbial contamination and nutrition are the biggies and food additives are not a significant source of actual risk to consumers, or at least not as much as they are perceived to be.

[END OF INTERVIEW]