



**Oral History Interview with
Jerome Halperin
Deputy Director, Bureau of Drugs
Assistant Surgeon General, Public Health Service
1971-1984**

**FDA Oral History Program
Final Edited Transcript
January 2, 2015**

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Oral History Abstract

Jerome Halperin had a distinguished career of public service that began as a pharmacist at the Public Health Service Albuquerque Indian Hospital in 1958, and included directing the Northeastern Radiological Health Laboratory in Winchester, Massachusetts (now the Winchester and Analytical Center), which was transferred to the FDA in 1971. Halperin served as Deputy Associate Director for New Drug Evaluation from 1974-1977, as Deputy Director of the Bureau of Drugs from 1978 to 1982 (after acting in that position for 1 year), Acting Director of the Bureau of Drugs from 1982 to his retirement in 1984 and as Assistant Surgeon General of the Public Health Service from 1980 to 1984.

Keywords

Bureau of Drugs; Bureau of Radiological Health; Public Health Service; radiology; pharmacy; United States Pharmacopeia; drug regulation; international relations

Citation Instructions

This interview should be cited as follows:

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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.

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Interview Transcript

JS: This is another in the series of FDA oral history interviews. This morning, January 2, 2015, the interview is with Jerome A. Halperin, retired Deputy Director, Bureau of Drugs, and Assistant Surgeon General in the U.S. Public Health Service. The interview is being held at the U.S. Food and Drug Administration headquarters in the Parklawn Building in Rockville, Maryland. The interview is being conducted by Suzanne Junod.

JS: Let's begin with your background up to when you started pharmacy school, where you grew up, what sort of a family life you had, that sort of thing.

JH: Interesting topics for an oral history of FDA. Okay.

SJ: Really how you came to be interested in the field you chose?

JH: All right. I was born in Paterson, New Jersey, 1937, moved to Passaic, New Jersey when I was about three years old, went to grammar school... Well actually, no. I guess moved to Clifton, New Jersey there. I was in Clifton until fifth grade. My dad owned a candy store, ice cream parlor. Moved to Passaic when I was in the fifth grade and lived there until I graduated from college and joined the Public Health Service.

Why did I go to pharmacy school? It's an interesting question because I never intended to be a pharmacist. I went to pharmacy school because of inadequate research and bad advice. (Laughter) I originally thought that I wanted to be a research biochemist. I thought that sounded neat. And I don't know why and I have no idea where that idea came from, but somebody once

said something about research biochemistry, and I said, “Gee, that sounds like that would be fun.” I couldn’t spell it, but yes, how do I do that? And I went to the high school guidance counselor – this was my first opportunity to find out that high school guidance counselors are usually totally worthless – and he told me that, “Well, the way you do that is to become a pharmacist.” Fine.

So I applied to several colleges of pharmacy including Columbia and Fordham and Rutgers. I came from a family where I had to commute to school. I was not going to be able to live away. And fortuitously I chose Rutgers – fortuitously because the other two are out of business, and it’s kind of embarrassing to be an alumnus of a non-existent school.

SJ: Kind of like the Emory Dental School? (Laughter)

JH: (Laughter) Yes, right. So I went to Rutgers. Rutgers College of Pharmacy at that time was up in North Newark, New Jersey and it was a four-year program. It took a year of pre-pharmacy and then three years of pharmacy. In my junior year I took biochemistry and found out it’s god-awful. I wasn’t the least bit interested in that. I also found out that I wasn’t the least bit interested in doing research work, because a researcher was in a laboratory and I was just too people oriented.

I remember coming home from school one day unhappy enough to think that I...I told my mother, “I’m going to drop out. I’m on the wrong track here. The last thing I want to do is be a pharmacist, and I’ve got to figure out what I want to do.” Well, she came from a Depression era family – she was the first born in the United States of a European origin family – and the idea that I would give up a scholarship and drop out of school that was just total heresy

and created a great ranting and wailing and tearing of hair and beating of chest: “Don’t do that! Finish! Get your pharmacy license, that way you can always make a living, always have a job, and then you can think of what you want to do.” And that’s what I did. I went back and decided, all right, I’ll finish pharmacy school, but I’m certainly not going to be a pharmacist, because the idea of standing there and making prescriptions didn’t appeal to me and the ideal of going into research didn’t really appeal to me. So I figured I’ll do something.

At the time when I was finishing school, in 1958, young men were still being drafted. This was post-Korea and pre-Vietnam, but there was still a draft. I didn’t want to get drafted, and I didn’t want to waste a couple of years driving a truck or doing some other silly stuff. And I remember that there was a required course – I guess every school’s got this – you know, the dean’s lecture series, you had to go. And there were two speakers that I remember – only two. They were both Public Health Service officers: the first one was Dr. George Archambault, whose name you know, and he came in wearing his uniform with four gleaming gold stripes, and here’s the Chief Pharmacy Officer, and he told us about the opportunity for careers and assignments in San Francisco and Seattle and Boston and New Orleans, all these great places. Gee, that sounds great. Two weeks later we had a fellow who had been in for two years and then left and he had been at a T.B. hospital for Indians in Rapid City, South Dakota, and when he got done we thought the last thing we’d want to go into Indian Health. That’s ridiculous.

But the idea of going into the Public Health Service appealed to me because I could get rid of my military obligation; I could be an officer; I might get a decent assignment for a couple of years and learn something about a hospital pharmacy. There were two of us in my class who decided we’d take the exams. And these were worse than state board exams. They were two

days. We went over to the PHS Hospital in Staten Island, and we spent two days taking written exams that were quite a bit tougher than the state board exams we took.

I graduated, hadn't heard anything, and I got a job as an intern at a pharmacy in New Jersey and got home one day and found that I had a letter from the Public Health Service saying that I had passed the exams. There were seven internships available that year, and I was number eight. I never thought I'd do that well. They said there were two things that they could do: number one, every year one of the seven drop out, so if I wanted to wait, there was a high probability I'd get placed somewhere. If I didn't they would offer me a staff assignment somewhere. And I found out that an intern has to spend three years, because the first year doesn't count toward your military obligation, but a staff assignment – two years and you're out. So I said, "The heck with the internship; give me a staff assignment I'll accept."

The next thing I heard was I got a telegram saying, "You are hereby ordered to active duty as a junior assistant pharmacist at the U.S. Public Health Service Indian Hospital in Albuquerque, New Mexico. And I reported there July 6, 1958 and found out that (a) it was a tuberculosis hospital, so all of the things I remembered from the fellow who had been in Rapid City kind of settled on me; and (2) I was the only pharmacist – it was a one-man station. I remember getting off the airplane and taking a cab and saying, "Take me to the U.S. Public Health Service Indian Hospital." And the cab driver said, "Is there one?"

SJ: That's when you knew you were in trouble. (Laughter)

JH: I said, "Yes, there is. Now the reason I know there is, is I know it's next to the County Indian Hospital." That's when I learned it was a T.B. hospital because he turned around and said

(whispering), “There’s a tuberculosis hospital there?” I gulped, and I said, “Well, you better that me there.” As an aside, when I got the orders to go to Albuquerque, the dean at Rutgers College of Pharmacy at that time, Roy Bowers, had come to Rutgers from New Mexico. So he told me... The only thing he didn’t tell me was that it was a T.B. hospital. But the hospital was at 801 Vassar Drive, N.E., and he used to live at 800, right across the street.

So, he told me that it was a nice little hospital. So at least I knew what to tell the cab driver. So I started out as an Indian Health Service hospital pharmacist and fell in love with a couple of things: one was public health – not pharmacy. As a matter of fact, as a professional challenge, it was pretty dull – one hundred and six beds, two wards, one operating room, and one clinic that had almost nobody that ever came to it. So I had very little to do, and I started looking around for things to do. That’s when I got my first real challenge and my first management position, because I was given the opportunity to provide pharmacy services to a couple of other hospitals, small ones, and health centers that did not have their own pharmacist.

I became like a little depot pharmacist; I ran a little drug depot, because I got their drug money and I’d buy and I’d prepackage and I’d label and what have you. I would supply the clinics at Acoma, Laguna, Jemez, Zia, Santa Ana Pueblos, along the Rio Grande, south to the Mescalero Apache Reservation, north to the Taos Pueblo just below the Colorado border, and to the Ignacio, Colorado health center on the southern Ute reservation. And I used to make the rounds. I used to get around to all these places, plus a couple of little places called Cañoncito and Alamo which were very, very isolated areas that a doctor went to only once a month on the Navajo, way out on the east side of the Navajo reservation. I got to see what public health issues were in dealing with Indians and the difference between that culture and ours.

The second thing I fell in love with was the southwest; I always liked that. I spent two years in Albuquerque, liked it very much, but professionally it wasn't going anywhere. I was offered two assignments at the end of two years. By that time I was an assistant pharmacist. Junior assistant pharmacist is what I was commissioned as – that was an ensign. An assistant pharmacist was a lieutenant J.G.

And I had two job offers. One was to go to Kotzebue, Alaska to be the first pharmacist at a brand new hospital in Kotzebue. Allan Brands, who was the Chief Pharmacy Officer for Indian Health at that time, offered me that job. And I said, "Oh? Tell me about Kotzebue. Where is it?" He said, "Well, a little bit in the north of Alaska." "How far north?" "Nome." I said, "North of Nome or south of Nome?" He said, "North of Nome." "North of the Arctic Circle or south of the Arctic Circle?" He said, "Oh, right around the Arctic Circle." I said, "OK." He said, "Yes, but not so cold because it's right on the water." I said, "Bering sea?" He said, "Yes." I said, "Oh, thank you very much." I said, "Al, tell me about Kotzebue." He said, "Very, very nice place." He said, "A real beautiful hospital." I said, "Very nice, who lives there?" He said, "Oh, an indigenous community." I said, "That's nice. That means Eskimos, right?" He said, "Yes." I said, "How many non-Eskimos?" "Ten." I said, "It gets dark there a lot, doesn't it?" He said, "Yes." I said, "Al, I'm not married. (Laughter) You know, I don't think I ought to go up there or I'm going to go crazy or go native. What else have you got?" (Laughter)

He offered me the job as chief pharmacist at the Indian Hospital on Fort Defiance, Arizona, which was a big one. It's still there and it's still pretty busy. And I said, "I like that," because that was a big station. I think there were four or five pharmacists already, and that was a nice job offer. But I said, "On one condition: I get living quarters. I want an apartment." He

said, “Well, you’re single, and because you’re single, we don’t have enough quarters for that. You have to live in interns’ quarters.” The interns’ quarters was a euphemism. You shared a bedroom with another single male officer in an old wooden frame house behind the mud alley from the back of the hospital, and you lost your whole rental allowance for that. I said, “Thanks, but no thanks.”

And as a result, I transferred into, at that time; it was called the Division of Hospitals and spent the year at the Public Health Service Hospital in Staten Island, New York, where I was one of about nine or ten pharmacist and hated every single minute of it, because all I did was type labels and put them onto a box. And it was just the most stultifying professional experience ever, and it convinced me that if this is what pharmacy is all about, I don’t want any part of it. It’s just not for me.

Well, when I had been in Albuquerque, two of the people I worked with at the hospital there went into radiological health, which was a new growing program in the Public Health Service. I mean this was a time of fallout. This was the time when you saw the *Saturday Evening Post* had – remember the *Saturday Evening Post* magazine? – had the cartoon of the lady going in to buy milk, and you’re wearing earphones, it reminds me, she had a Geiger counter with the earphones on and the detector over the milk case because there was a radioiodine in milk.

SJ: We have pictures of FDA inspectors checking fish, too.

JH: Well, it was an opportunity. They were looking for people with scientific backgrounds. Couldn’t get enough MDs’ they had enough engineers, but they needed people with biomedical

backgrounds, and they were willing to take pharmacists and train them in radiological health, radiological sciences. And you got to go to school, and I had wanted to go for an MPH degree. So I made a phone call to a couple of my former colleagues from Indian Health who had gone into radiological health: the two chiefs of the hospital in Albuquerque, believe it or not; one went to the regional office in Denver and the other one came in here at headquarters. And I called him up and I said, "I want in. I want to go to school." And to make a long story short, I got to go to Johns Hopkins for a year and get an MPH – also got an M-R-S; met my wife there.

SJ: At Johns Hopkins?

JH: Yes. So I spent, then, fourteen years in radiological health. My first assignment, after getting my MPH was three years assigned to the California State Health Department where I did everything. I wrote radioactive materials licenses for health care groups, for industrial groups; I did inspections; X-ray machines; environmental radiation. My assignment was essentially to be an intern and to learn everything about how a state runs a radiation control program. And after three years, I came back here and I worked in the building right across the street, the Chapman Avenue building for a year as a liaison. I set up a program, a function, where I was the liaison between at that time – what was it called? – the National Center for Radiological Health – that was one of its incarnations – and the states that were agreement states, those that held authority from the Atomic Energy Commission at that time, before the Nuclear Regulatory Commission, to license certain kinds of radioactivity.

I got a letter one day. But, by the way, I loved the people. I worked with John Villforth at that time; he was the Branch Chief. John and I became friends then. We're still close friends

to this day. But the job was dull. I wasn't active enough; I wasn't doing enough. One day a letter comes from the State Health Director of Kansas saying, "We have just lost our staff. It resigned, and we are in jeopardy of losing our agreement with AEC—Kansas was the ninth agreement state – will the Public Health Service assign someone?"

So I wrote a letter: "The Public Health Service is happy to assign Jerome A. Halperin," and put it in front of John's boss, a fellow by the name of Howard McMartin, who was the physician head of that division. I said, "Sign here." And Mac looked at that and he said, "Is that what you want to do?" I said, "You bet, that's what you trained me for in California." He said, "Call them up. Tell them you want to come and talk to them." I went out, and I essentially cut my own deal. I essentially ... They were over barrel, and I was able to dictate the terms that would work for. They weren't paying my salary, but I said, "These are the responsibilities and authorities that I want; these are the freedoms that I want and the prerogatives," which weren't unreasonable, but I wasn't coming in to work for some state guy who knew less than I did. I worked for a gentleman out there, now deceased: Lee Mays. And he said, "Sounds perfectly reasonable to me. Fine."

So my wife and I moved out. She was seven months pregnant at the time with our first daughter, and our 180-pound Great Dane was along, too. And we took up residence in Topeka and were there for two years and really liked it. I ran the radiological health program. I recruited and hired my replacements. When I was done with that and I thought it was time to go, the state health officer said, "If I can set it up with your boss, would you stay and run the occupational health and air pollution control programs for us?" And I said, "Sure." And I did that for the last six months, because I had had some training in industrial hygiene and occupational medicine at Hopkins. And did the same thing. I wrote the air pollution control

grant application for them, and Kansas got the first demonstration grant for an air pollution control program. I attended the first air pollution control hearing in Kansas City as part of that process. Set up the ... well didn't set up, but I recruited somebody to run the occupational health program after I had been, you know, keeping my finger in the dam for a while.

Then I left and went to the regional office in Chicago for the Public Health Service where I was Regional Radiological Health Representative for the Great Lakes States, and then became the Environmental Control Director. That's when there was such a thing called the ECA. In the Public Health Service there was the Environmental Control Administration. It was parallel to the National Air Pollution Control Administration before the Environmental Protection Agency (EPA) was created. I ran radiological health, occupational health, solid waste management, water supply, and something called community environmental management. I did that for three years.

Right at the tail end of that is when EPA was created, and the radiological health program of the Public Health Service was split in half. The environmental parts of it went to EPA; the biomedical parts went to FDA. I was on the list to go to EPA; my deputy, who was an engineer, was on the list to go to FDA, and we swapped. I said, "You'll do better in EPA as an engineer; I'll do better in FDA as a pharmacist." I stayed with the FDA part. Now we were part of – I don't even remember what we were called then – it might have been the beginnings of the Bureau of Radiological Health. John Villforth had been named the Bureau Director at that time.

SJ: What do you remember about that? That transition is something I'm not very familiar with, but was it a smooth transition? Well, anything that you remember about that period would be helpful.

JH: No, Why don't we come back to that. I'll bring you up to the current, where I got here, and then we can go back to that. I went up from Chicago to Winchester, Massachusetts.

SJ: WEAC (Winchester Engineering and Analytical Center, Winchester, Massachusetts).

JH: Yes, at that time, well, it wasn't WEAC; it was NERHL, the Northeastern Radiological Health Laboratory.

SJ: Oh, good, thank you.

JH: Because there were three laboratories that were part of the old National Center for Radiological Health: one in Montgomery, Alabama; one in Las Vegas – those were both only environmental radiation labs, and they went to EPA. The one in Winchester, Massachusetts, the building was owned by the Department of Health, Education and Welfare (HEW). It was not a GSA building, so they decided that one would stay with FDA. The major programs there were still environmental radiation, and I was sent up by John Villforth to make that into a medical X-ray protection laboratory. Over the next two years, we did that, during which time I wound up evicting, essentially, the EPA component, and they moved down here and to Alabama, so that we could have the lab entirely to ourselves and to convert some of the old uranium chemistry laboratories.

The laboratory was originally built by the American Cyanamid Company under a contract and then run by National Lead Company, and it was a uranium purification technology lab. Once they completed the contract for the AEC and figured out how to do that, they got a ... The contract was over; AEC didn't need the building anymore; it was declared surplus; and the Public Health Service picked it up because it had something to do with radiological health, and they started to use it.

SJ: It was a well-made lab, if I remember correctly.

JH: It was an interesting place. It was well-made for its original purposes. But you never saw the lab at the time it was still an environmental lab. There were old chemistry set-ups that we used for uranium separation that nobody needed anymore. We wound up tearing those out. We had the best group of scroungers in the world up there. There was a permanent staff who was hired by HEW that originally worked for National Lead or Cyanamid and National Lead under the contract and they stayed on. They knew the building upside down and backwards, and all of the stuff in the back yard, in the warehouses, they had picked up from military surplus. We had tons and tons of lead bricks.

SJ: Yes. I remember. They showed me something when I was up there that they had gotten some pre-World War II steel they used to construct something.

JH: Oh, the cannon barrels. We had pre-World War II cannon barrels, made with thick steel. There was no cobalt 60 in them so we used them as shields against cosmic radiation when doing

low level counting. Most of them wound up being shipped down to Alabama. But, because we had no money, we traded lead brick to a lead dealer who gave us lead sheet, which we put up on the walls and put nice paneling over it; so we made shielded rooms for X-ray work. We did that with a couple of rooms. Then we put in a radioisotopes laboratory when nuclear medicine started to get busy. So we had a very nice radiation protection lab, but not enough money to run it.

It was at that time that the Bureau of Radiological Health couldn't support it anymore, and they traded it off to Executive Director of Regional Operations (EDRO). I didn't at all want to work for EDRO. I just thought that was an organization where I would go nowhere fast, and John offered me an opportunity to go to school again. He came up one day and he said the whole deal was done.

As an aside, the laboratory could have stayed with that group, because John had been asked by Charlie Edwards, who was Commissioner at that time, to take the Medical Device Program. And I begged him. I said, "Take it, please. Put it up here. We've got a laboratory; we've got a facility for it. This would be just the place." He didn't want to do it. He was worried that if he did that; Devices would become more important than Radiological Health. To which I said, "Yes, they will. They should."

He didn't want to do that. It was going to contaminate Radiological Health. In retrospect, it's too bad, because that could have been Centers for Devices and Radiological Health (CDRH) lab right now.

When the deal was done and the lab was set to go to EDRO, John knew I didn't want to do that, and he didn't have a job for me down here. When he came up to spend the day with me, he said, "Look, there's a six-week program at the Massachusetts Institute of Technology (MIT).

Why don't you go to MIT for six weeks? By that time we'll probably be able to figure something out. Talk to somebody there, give them a call.

So I called and they were already expecting my phone call. So I looked at John. I said, "Not wired, right?"...Okay, you're going to be here for a couple hours?" He said, "Yes." So I went down there and talked to them at MIT. I came back and I said, "John, you're absolutely right. MIT's the place I should be. There's only one little difference." He said, "What's that?" "The people at MIT really believe this six-week program is not the appropriate program." "What is?" I said, "The Sloan Fellow's Program." "What's that?" It's a one year, twelve month program with a little required travel. How much? "A week in New York, a week in Washington." He said, "That's do-able." "Three weeks around the world." (Laughter) He looked at me and said, "I think I've been had." I said, "Well you know, you're making me an offer I can't refuse and I'm making you one you can't refuse, so let's work it out." John made it happen, and I got to go to MIT for a year as a Sloan Fellow.

Indeed it was one of the most wonderful experiences of my life. I was in the last all-male group, fifty of us with an average age of thirty-six. All of us had been in some lower-to middle-management positions. Fourteen were from government; about fifteen were non-U.S. people. It was really a wonderfully mixed group. As I said, we spent one week in meetings in New York, one week in meetings down here, and we got to go around the world for three weeks. It was a required part of the curriculum. The only thing we had to do was you had to turn your thesis in before they'd let you on the airplane. (Laughter) There was one guy who turned it in that morning, and we went to London, Paris, Frankfurt, Berlin, Leningrad, Moscow, Tokyo, Kyoto, and back home to Boston.

When I was done with that program, John said, ‘I don’t have a job for you at the level of a Division Director. ‘I’ll tell you what. I’ll give you a hunting license. Take all the time you want, I’ll cover for you. See what you can find.’ I said, ‘Fine, I’ll do that.’ And the next thing, he called me up and said, ‘I’ve got a lead for your.’ He said, ‘The Bureau of Drugs just got an opening for a Deputy.’”

[BREAK]

JH: He said that a fellow by the name of George Leong had been Marion Finkel’s Deputy in what at that time was called the Office of Scientific Evaluation in the Bureau of Drugs, and he had just left and they were looking for a replacement. He said, ‘I think you ought to call about that.’ So I made a call and said, ‘I understand that job is open. I’m a pharmacist just finishing MIT with fourteen years in Rad. Health.’ ‘Come on down and talk.’ I was interviewed by Marion Finkel, Carl Leventhal, and Dick Crout, and got the job offered the next week. There in 1974, some sixteen years after I had started my pharmacy career, I came back into pharmacy in a broader context. I was back in the realm of drugs.

I spent July ’74 to December ’77 as Deputy Associate Director for New Drug Evaluation (Scientific). It’s the longest title I’ve ever had. I was Marion Finkel’s Deputy, and everything that had anything to do with the operations of those divisions, other than the actual approval of the new drug applications themselves, I could get involved in, and do what I wanted to do. It was a question of making my own job, and I loved it. I have a great relationship with Marion, Carl Leventhal, and Dick Crout. I went to Tokyo one year with Ted Byers, who was the head of Compliance at that time. We were the first Bureau of Drugs people to go on a bilateral meeting

after who was it? – Commissioner Alexander Schmidt, I guess, had been the first one over there the year before to establish the ministry of health contacts.

When Carl Leventhal had a heart attack in the fall of '77 and decided that he was going to go back to the National Institutes of Health (NIH) and do something with less pressure, Dick Crout asked me if I would be willing to be Acting Deputy while they were looking for a new Deputy Director, and I said, "Okay." A new administration, Don Kennedy came in January, 1980 as the FDA Commissioner. Somehow Dick never got around to recruiting for a Deputy. Towards the end of 1980, I went to him and said, "It's time we talked here. Are you ever going to recruit for a Deputy or not?" He said, "No, why should I?" I said, "Well, then if you're not going to do that, I want to be confirmed. I want the 'Acting' taken off my name." He looked at me and said, "I totally forgot it was there." So he called Don Kennedy, and it was a matter of a couple of days before the orders were cut and I became Deputy Director in my own right.

The best years I have ever spent were from December of '77 until around summer of '82 when Dick left. I had never had the pleasure of working for somebody whom I respected more and from whom I learned more. I've always believed in mentorship's and I've always done well in mentorship positions. I've worked for people in California and other people in the Public Health Service, you know, of mentorship relationship, but with Dick it was unreal. I mean, he and I just meshed, because we complemented each other in background and skills. In fact, we were probably a better team as Deputy and, Director than he and Carl Leventhal were because they were both physicians and they would occasionally disagree on whose medical opinion would hold sway. We never had that.

Dick Crout was the kind of guy who said, "If you can do it, do it." He wasn't unwilling to delegate anything. But if you stood around and said, "Can I do this?" It's unlikely that you're

going to get an answer. The one thing you don't do with FDA is ask, "Can I do it?" You just do it, and if someone doesn't like it, they'll tell you – they'll tell you quickly enough. But if you just do it, and you're doing it well, they applaud that. They don't have to do it anymore.

I worked with Dick until he left the Bureau, and I was really sorry to see him go. I remember him and his wife, Carolyn, and Barbara and I were out to dinner at a restaurant in Ellicott City (Maryland) one Saturday night, and he said, "How would you like to be the Director of the Bureau?" And I looked at him, "What did you say?" He said it again. I said, "What are you telling me?" That's when he told me he was leaving. I was just dumbfounded.

I said, "The quick answer is no, I don't want to be the Director." "It's flattering that you even think that somebody might seriously consider me for that job." "But I know my strengths; I know what I do well and what I don't do well." "I am a terrific Deputy; I think you'd agree with that." And he did. I said, "But I would not be a terrific Director, not for this. "I think you need those two initials, M and D, after your name. "I'm not saying a pharmacist couldn't do it, but, I think it would be a lot harder. There are just too many opportunities to get sniped at," which he agreed with. I said, "But what I do want to do is tell the search committee what I think they ought to be looking for."

SJ: Had the person in this position always been a physician to your knowledge?

JH: There had only been one Bureau of Drugs Director – Dick Crout. Before him there was a Bureau of Medicine Director, who was Henry Simmons, also a physician. So, yes it always had been a physician. Now, before that, in some other construction of the organization that I'm unfamiliar with, I don't know. But I believed then and I believe now that the Director of

whatever the organizational component is called that's responsible for drugs should be a physician. I think that job is more important to be a physician than commissioner. And I did talk to the search committee. In fact, that's where I got to meet people like Art Hayes and Jim Doluisio. Interesting, Art Hayes is the President at the United States Pharmacopoeia (USP). Jim Doluisio and Dick Crout are members of the Board of Trustees. Good people hang around and do important things with more than one organization. I did talk to the search committee and I did tell them what I thought they were looking for in a replacement for Dick; I basically said, "It's got to be somebody a lot like him, who thinks policy, and medical health care policy as well as federal regulatory policy – somebody who is a broad thinker. Not just a scientist, because, I think that somebody who's a pure scientist, but doesn't have that understanding and grasp of federal health care and federal regulatory policies, will not do well."

After a very unsuccessful, long search, Art Hayes finally, and I think somewhat reluctantly, asked Hank Meyer to turn a combined organization of Drugs and Biologics. Art asked me if I could stay for a while and help Hank set it up and run it. I agreed to do that for a while but with no long-term commitment. After one year, I had decided that it was just not a situation I wanted to continue. Hank was not a bad man. Paul Parker is a gentleman and a good scientist. Hope Hopps, who had come over with them, was a very honorable person. But the traditions of the organization of Drugs were so different from that of Biologics that it was an oil and water situation right from the start, and I did not agree with the policies or the procedures that they were putting into place. I just felt that they were making some changes without understanding what they were changing from and why it was the way it was. And they were in the long run likely to do more mischief than good.

I decided that after twenty-five years, and I'd gotten up to be an Assistant Surgeon General (ASG), I was as high as I was going to go anyway. I could stay and grit my teeth and wait out another few more years and retire with a little bit more money, and I thought I've never worked for money in my life, and why do it now? Life's too short.

I've got a couple of principles about work that I live by. One is that it's got to be fun, and if it's not fun, don't do it. Work had stopped being fun. The second one is that when you think you are contributing more than you are deriving intellectually, so that the tip of the intellectual scale is balanced against you, it's time to leave. And the third is, you leave when your departure is met with regret rather than relief. And I thought that all of those had crystallized, and it was time to go.

I guess, very fortuitously, I had come to that conclusion and I was talking to my wife at dinner one night and I said, "I'm going to start looking around." The next day my secretary, Betty Palsgrove was away and the phone rang and I picked it up. It turned out to be a recruiter. Now she used to screen all my calls, and she had standing orders: if a recruiter called, don't put him through, I wasn't looking for a job; I didn't want to talk about it. I wasn't going to give references if that's what they wanted.

It turned out it was a recruiter. When she identified herself I was about ready to hang up, and she said to me, "Are you so goddamned important that you can't spend five minutes listening to something that may be a superb opportunity for you?" And I thought, "Lady, you've got more brass than a bazaar in the Middle East." I said, "Okay, five minutes." Well, in five minutes she described a job that sounded terrific. Didn't tell me what the company was, just described the job. And she said, "Okay, five minutes is up. I'll hang up if you're not interested."

I said, “Okay, you hooked me. It does sound interesting.” I had already concluded, literally, the night before that I was interested in looking around.

So she said, “Okay, I’ll come down in your office.” I said, “Nope. No, you won’t. If you want to come down, fine.” We met in the cocktail lounge of the Holiday Inn in Bethesda, Maryland. When I walked in – it’s around 1:00 in the afternoon – she was the only person there. I said, “Are you so-and-so?” She said, “Yes.” I said, “Okay, I’m Jerry Halperin.” She said, “This is a lot of fine intrigue.” I said, “Yes, it is. You are obviously talking about a drug company, and I regulate it. So we have a little bit of a drill to go through here. It’s kind of a ritual. “Number one, don’t tell what the company’s name is, because the minute you do, you bias me. “I’ve already figured out that it’s a company in the Northeast and probably in New Jersey. And I’ve probably got it figured out that it’s one of three. But I don’t want to know any more than that. And don’t talk to me about money. Tell me what the job is.”

We spent about two hours, and at the end of two hours I said, “Yes, I’m interested in going further.” She said, “Fine, I’ll send you a plane reservation.” I said, “Don’t do that. Let me go back to find out what the next step is, because I want to limit my exposure so that if I decide I don’t like it, I’m not in a position where I have to step back from anything to do with this company because I’ve been essentially tainted.” So she said, “Well, it sounds like a lot of hocus-pocus, but okay; I’ll go back and I’ll tell my client.” I said, “Okay, I’ll call you when I’ve got it figured out.” And I went back and I talked to Tom Scarlett and Jess Stribling. I told Tom, “There’s a job offer I want to listen to. I know what the title of the job is, but I don’t know the name of the company yet. I haven’t done any negotiating. How do I do this legally?” And he said, “You have come to the right place.” The expert is Jess Stribling, and Jess came in and he described exactly how I should go about it: “You can do anything you want, until negotiation,

before you have to let anybody know officially. So if you want to go up and talk to them at this point, you can do that. You've let us know and that's enough."

So I called the recruiter, and she told me it was Ciba-Geigy. I said, "That was one of the two that I figured it was probably going to be."

She said, "I'll send you plane tickets." I said, "Nope. I will pay for this out of my own pocket." "It's easy. I can drive to New Jersey. This way, if I don't like it, I didn't take a nickel from this company." She said, "It's from our company." I said, "No, it's not, they're paying you. Let's do it my way." So I went up and I met with the people at Ciba, spent the whole day, and at the end of the day I concluded that it sounded good. The president was about ready to make me an offer and I said, "Please, don't do that." "I have to find out how I can do this legitimately in the next step. So let me go back and talk to the general counsel again."

I had to put a note in the file that I was negotiating with Ciba-Geigy and that I was disqualifying myself from anything that had to do with Ciba-Geigy. Interestingly enough, I had just signed a regulatory letter to Ciba-Geigy two days earlier and handed it to a vice president who was down for a meeting. Therefore, if I had known it was Ciba-Geigy before I went up there, I couldn't have done that. The letter I wrote was counter-signed by Voyce Whitley, who at that time was the head of Conflict of Interest staff, and Gerry Meyer, who at the time was the Associate Commissioner for Management and Operations (ACMO), and one other person had to sign it. Then I could go up and we could negotiate.

I accepted a job offer, and so I had to put in for retirement. They wanted me to start in two weeks. I said, "Whoa, I am a commissioned officer. It's going to be three month's minimum, and that's only because I'm an ASG and I don't have to go to a retirement board." They were willing to wait three months. We were able to keep it quiet for two of those three

months before it finally leaked that I was going to Ciba-Geigy, and then I confirmed it. I retired on June 1, 1983, joined Ciba-Geigy, spent six years with them, and now I'm down here.

But I had twenty-five years with the Public Health Service, and about thirteen years with FDA because I came into FDA after Rad. Health and EPA was created. (It was Federal Reorganization Order #3 under the Nixon administration), plus nine years for the Bureau of Drugs.

I guess that the creation of EPA was harder on Rad. Health than it was on any other component in the federal government. The reason I say that is that only Rad. Health was divided in half. I mean Solomon literally had to cut the baby. All of their pollution control went. All the water pollution control went. All of solid waste management went. All of occupational health stayed. Rad. Health was cut in half, almost exactly a 50/50 split. It was not the kind of a division that was easy to live with. It was easy when a whole building went: when the whole lab in Las Vegas went, when the whole lab in Montgomery went. They were all gone. It was very difficult in New England, and that was one of the reasons that I really insisted that the EPA group leave. It was very hard, because that was a group that had been together for a long time. Many of those people had worked together for almost twenty years, and when some of them had to leave, it really tore them up.

And it was, "Who owns this machine and this instrument? This is mine. You're going to put this over here and this is going to get shipped to Alabama, or this is staying here with us." It was very uncomfortable. The research lab had a line right up the middle. It was the Berlin Wall: EPA/FDA.

SJ: A little hard to manage, but...

JH: Yes, well, it was more...I guess you said the right words. It was impossible to manage. It had not been thought out well; you know the lines from Hamlet, "If it were to be done 'twere well that it be done wisely and swiftly." If somebody had said, "Load it in the truck and by Monday morning you and your instrument, or half of it, are out of here," it's one thing. But to try to live with that, with this invisible wall: this side is mine and that side is yours – don't come across. I don't work for you anymore – you can't tell me what to do. I don't know who my boss is – he's not here. It was difficult. It was not so difficult out in the field.

As I said, there were three of us in the Chicago Regional Office who were there for Rad. Health. I was there, Mike Conlon, who was my Deputy, and Leon Zellner. Those two wound up going to EPA. No, I'm sorry, Mike went to EPA; Leon stayed with FDA, in fact, then went to the Dallas Regional Office as an Assistant Radiological Health Representative; and I went up to Massachusetts.

The split took too long to finish, and there was a great deal of unhappiness in there, especially when some of the new programs, for example, the microwave radiation programs were really getting sorted out as to who does what. The Federal Radiation Control for Health and Safety Act of 1968 finally gave FDA the authority over electromagnetic radiation. Okay, that's 1968. We had just gotten that act, really didn't even have the regulations, didn't really know who's doing what or where, and now we had to divide it up, who does what. Because there are some things that are environmental and some things that are not. The microwave, the transmissions for radio telephone, the long-wave telephone: there are environmental radiation programs, not the occupational or medical radiation programs. Part of the early microwave group [in fact they were housed in some quarters on the Forest Glen campus of the Army, the

Walter Reed campus] went to EPA. The Stone Street Laboratory was the first X-ray lab. It was an old garage essentially. That stayed. In fact, some of that went up to New England, some of it went to Chicago, and later it was put together here when they finally got the Twinbrook complex.

It was a difficult transition period, and I think that for a while there were some very hard feelings on the parts of individuals who felt they had been betrayed. The commissioned officers especially felt that they had really been sold down the river. And in truth, when you look at the history of the Commissioned Corps in EPA, it's been one of attrition. EPA has suffered those people, but now most of them are retired. I don't know how many EPA officers are still on active duty.

SJ: Well they are just celebrating the Commissioned Corps Centennial this past year, so I've had some involvement with that, but one of the motivations behind reenergizing the Corps, so to speak, is to make it mobile again. But I gather during the period that you're in, that wasn't ever considered part of it.

JH: Well, the whole idea of mobility of the Corps is kind of cute. How mobile is Ed Martin? Ed Martin is the guru of the program to revitalize the Corps, you know, appointed in that position by Surgeon General Everett Koop. I don't know that Ed's moved around. When you get to certain levels, you don't have the availability of positions to move around. The military even finds out that just moving people around for the sake of moving them around is pretty expensive and pretty wasteful. That's one of the reasons that a lot of jobs that military people had years back are now civilian jobs; and the military people, more and more, are people who are

the fighting people. The Indian Health Service was always mobile, especially at the lower levels. I mean it's when you got up to be Chief of Service that you kind of stayed around in one place, but otherwise you moved around. Even the Bureau of Medical Affairs, which ran the hospitals, before we started getting rid of them and closing down all these hospitals, had a lot of mobility. World Health Organization (WHO) wasn't mobile, National Institutes of Health (NIH) wasn't mobile, and people here in headquarters – they weren't then; they're not now. Because to me, it's not mobile if you take a guy and you move him from the fourth floor to the second floor of the same building and say, "See, he's transferred."

SJ: In the midst of this they said that the Corps' ideal of mobility was moving from Rockville to Silver Spring and back. (Laughter)

JH: Did you tell me that John Villforth said in twenty-six years he's moved three feet?

SJ: No. (Laughter) Well, it sounds like they just predicated this on the wrong basis in one sense.

JH: I'm not trying to be very cynical, because I think that there's a lot in that need to revitalize this Corps. To make the Corps people understand that they're not civil servants. They're different. And I agreed with that. I had been one of the guys who started wearing a uniform one day a week in the Chicago Regional Office. I always wanted to wear the uniform, because I felt that that was an important symbol. It also made me feel good. So I'm glad to see that the Corps is in uniform and that they're thinking more like they're different. You should

have seen what some of the guys in uniform looked like at this Staten Island hospital. Some of those guys, especially the medical interns, I don't think they ever washed the uniform, or they must have slept in it. They looked terrible. When they'd go on the Fort Wadsworth Army Base they looked disgusting and they were an embarrassment. I think it is very appropriate to wear the uniform and wear it according to military etiquette.

SJ: How long did the transition take, do you think?

JH: For Rad. Health? Oh, a year, year and a half.

[BREAK]

JS: Do you have any comments or feelings about how effective the program was before and after the transition?

JH: I don't think it made any difference, because there had been a lot of enthusiasm and activity in the medical X-ray, microwave oven, the TV activities before the split, and I think that continued unabated, because the people who were doing that continued to do it. None of the people who were doing that went to work on environmental radiation with EPA. None of the people who were doing environmental radiation came to work on microwave ovens or TV's or medical X-ray. So I think that a much, much smaller group kept doing what they were doing. And I think that they did not lose any efficiency.

I thought that Rad. Health was a very small bureau at that point. There must have been only three hundred people in it or less. The Bureau of Foods and the Bureau of Drugs, were mammoth compared with Rad. Health in those days. I think Rad. Health was no bigger than Vet. Med. – very, very small and equally specialized and very ill at ease being put into FDA.

There was another part of the transition that was difficult. Before it went into FDA, Rad. Health was floating, literally. It was assigned directly to Roger Egeberg, who was the Assistant Secretary for Health. It was a national center without an umbrella organization, because the umbrella organizations had all been essentially shifted.

Rad. Health was stuck in FDA, and we hated it because FDA is a compliance regulatory organization. At that time, Rad. Health had the Radiation Protection Act, and the Radiation Control of Health and Safety Act. It was more of an educational program, and it worked by education and persuasion. There was no such thing as regulation. We didn't even have the regulatory power. So we were really ducks out of the water in FDA, and I can remember that before I went up to Massachusetts, I was assigned directly to the Regional Food and Drug Director in Chicago, who at that time was Don Heulton.

Don was a gentleman, and he knew that this was an unusual situation for me. Here I had been the Regional Environmental Control Director with a half a dozen programs under me; now I was a one-man band essentially working for him. He knew I was negotiating to get out of that and go up to Massachusetts, so he let me alone as much as possible but he told me, "Look, there are some things you're going to have to do, especially with regard to travel and reporting arrangements." It was the first time I'd ever realized I was right under somebody's thumb, because that's how EDRO Executive Director of Regional Operations (EDRO) operated.

And I couldn't stand it. I had nothing against Don. Don and I were always on very, very good terms when he and I were both down here. But I knew I didn't want to work for EDRO. And that's why when the Northeast Radiological Health Laboratory (NERHL) went to EDRO, I got out. So I think that that transition for FDA was particularly difficult for Rad. Health into FDA. I marvel that John Villforth was able to keep it together and keep his spirits up and keep the morale up. I think he did a very, very good job, because he was under a great deal of pressure himself, especially because of the people in the field.

There weren't very many of the Rad. Health people. In the early sixties when I was out in California there were, at one time, maybe sixty or seventy people assigned to different state simultaneously. We had six in California at one time. In the Regional Offices where we had one or two or sometimes three people. And now there are virtually no more state assignees and the people in the Regional Offices were really working for the Regional Food and Drug Director, not for John Villforth. But John was a good diplomat and he managed to keep the program together. I don't know what those guys are doing out there right now. I have no idea; I've lost track completely. I do know that they wound up being in dead end positions, because they were neither fish nor fowl. They were not part of the EDRO organization. They weren't investigators. They were not accepted by the people in the districts. There's no home for them back here; they couldn't get back here. Some of them eventually got transferred back here.

So out of that group that was in the states and in the Regional Offices, I probably did as well as any of them. I was able to get into a laboratory job and then into another bureau where I became assimilated, more a part of FDA.

SJ: That was as much due to your pharmacy background as your other office time. You just had...

JH: But there were lots of other pharmacists. We had a lot of them in Rad. Health. If you go back and look at the history of Rad. Health you'll find that there must have been twenty or thirty pharmacists in Rad. Health at any one time. Right now, I guess Mark Barnett may be about the only one left across the street. But there were people like Bernie Schly and Frank Barletta and Don Heir.

JS: Why do you think so many pharmacists went into Rad. Health?

JH: Oh, easy: they couldn't get physicians. They were looking for people with biomedical backgrounds to balance the engineers. Somebody said, "Why don't we try pharmacists? We've got a lot of them." They sent us all to either Schools of Public Health or to short courses. When I finished at Johns Hopkins, I spent the summer at the Robert A. Pabst Sanitary Engineering Center in Cincinnati, and at Oak Ridge, and they found out that we did very well. We could keep up with the science. We could bring some of the biomedical skills on radiation effects that they couldn't get because they couldn't hire enough physicians. And they got us out of the pharmacies, gave us a whole opportunity for different careers.

SJ: Well, I guess we can move then into the drugs area. You were mentioning before we started the tape that there were several activities that started up just as you got there. So just take them in order and get them on tape.

JH: Okay, I showed up in early July of 1974, and I remember in the room next to my office, Dr. Allan Bone was working on drug lag testimony that was supposed to be delivered by Commissioner Schmidt at the hearing before Senator Kennedy on August 16, 1974. That famous and very interesting testimony which was submitted in writing for the record was never read into the record, because Senator Kennedy surprised Commissioner Schmidt by a parade of conscientious objectors: employees of the Bureau of Drugs who were saying that they had been treated unfairly and unjustly, that they had been transferred from their jobs, that all this was being done to placate industry, and that FDA Bureau of Drugs management was bad. That started an enormous investigation. It started out with Dr. McMahon from Tulane who was asked to chair a group to look into these allegations. That didn't last very long. That commission failed for a variety of reasons. I think (1) McMahon didn't want to do that; (2) the charge to them was not clear; and (3) he was a physician and didn't think it was very important. It became the Dorsen panel. Mr. Dorsen was a lawyer from New York who approached it in a much different way. He had the Inspector General involved at that time, and he had an investigative staff. They looked at several different aspects. One was the processes of new drug evaluation. The other was under a man who I think was probably an ex-FBI investigator; he was looking into potential criminal actions with regard to how these employees were treated.

Senator Kennedy came at this from the point of view that most politicians in his position would be as a committee chairman with the TV cameras rolling: "FDA's guilty; the employees are right." It took FDA years to try to put that into perspective. I think that in retrospect the Dorsen Report and the Commissioner's rebuttal to that, which Bill Vodra, another guy you've got to talk to on this, was personally responsible for and which he wrote, just gave the thing more

value and made it more believable than it was. “Me thinks thou doth protest too much,” is what my reading of all of that was after it was all over.

I put a set of all of the hearings, and there were several, dealing with the conscientious objector question. They were the hearings; there was the Dorsen Report; there was the Commissioner’s response; there was the Government Accounting Office (GAO) report that was also a part of that. It stood about that high, and I sent that off to Dr. Ed Shein at MIT in the Department of Organizational Psychology, and I said, “If you ever get a graduate student someday to look at this, there’s something that ought to be learned from all of this, this self-flagellation that was going on.”

Because if you look dispassionately at each of these cases, yes, some of the people were transferred. They were transferred out of positions they had been in to other positions. Why were they transferred? Because some of them were absolutely not doing their jobs, and for a variety of reasons the institution was not dealing with them properly. They should have been fired, but I will tell you something; they couldn’t do that. You couldn’t fire these people because there was a lack of will and a lack of spine, at least steel in the spine, but the institution helped do that. Some of these people were so incapable of doing a credible job of drug evaluation and being dispassionate and unbiased about the data. Some of them were just anti-industry. Some of them were just so poorly prepared for their jobs they shouldn’t have been in them. Some of them were just plain obstructions. They thought it was the colony of the damned: put all of these people into this one group and send them to the moon, give them something useless to do. It wasn’t that. They were all put into other jobs, but a lot of them harbored notions that they were really unfairly mistreated.

One case that sticks out in point involved a physician, and I won't use his name; but it's the reason that Dr. Merle Gibson and Dr. Bill D'Aguano ("Dag") both received letters of admonition. If you knew Merle Gibson and Bill D'Aguano, there are no two people who are less likely to have treated somebody unfairly or poorly. Merle Gibson, around 1974, was the Director, and Bill D'Aguano, I believe was the Chief Toxicologist for New Drug Evaluations (NDE), magnificent man, died about '82 or so, was Deputy Director. They took an New Drug Application (NDA) away from an MD because according to Bill and Dag, as he was called, this MD told him that he doesn't care what the company submits in the way of data, he would never ever approve the NDA. See, now in a situation like that today, FDA would be expected to reassign that to somebody else, and investigate it thoroughly. I don't know if they did an investigation at that time, but they said, "Look, we've got to assign the drug to somebody who is less emotionally involved."

There were several things, several examples of things like that where people who were just too poor in terms of their ability to do their job in a dispassionate and intelligent way were reassigned. These are the people who then became the conscientious objectors, and their stories were given enormous credibility by the way it was publicized at the hearings. The investigation was put into a lot of this. I got personally involved in it because of a clerical error. It brought into this another physician who had not been part of the original group and who brought me into it.

During this time, there were several other things going on. In the 1972-73 period, Dick Crout was Bureau Director. The Auerbach Company, the big consultant group, was doing the Auerbach Study, looking at essentially the NDA review process and how at that time the new drug evaluation function was organized. There was a group that was created called the Auerbach

Implementation Task Force. We had a report and we were trying work through some of their recommendations to see which ones made sense, which ones were good, and which ones we ought to try to implement. A lot of things were going on.

For example, some of those recommendations were good: to decentralize the eighth floor document room so that there's more ready access to documents and things don't get lost and things move faster. Moreover, the building was literally going to collapse if we kept putting stuff on that eighth floor document room, because when I saw that, I couldn't believe what it looked like. It took up the back half of the B wing on the eighth floor, and it had every IND and every NDA and every supplement and every master file in it. I didn't know how the building was standing up either. The building inspectors were very concerned about the floor with that much weight. It was just impossible to work there. There are photographs of that.

The model division was supposed to be neuropsychology, neuropsychiatry, and neuropharmacological drug products. It was HFD-120. That was I think the first of the decentralized document rooms; then surgical dental up on the eighteenth floor was the second one. They've gradually decentralized all of the document rooms, which was supposed to make it better. I don't know if it's any better or not, because by the time I left, we had the same kinds of troubles with six different document rooms what we had with one. There was just too much paper and not enough people to take care of it.

This is when we got into all of this business, because we had a bunch of personnel things going on at the same time. We were trying to look at the correct job classifications and pay grades for the document room clerks, because the personnel people went a little more by GS-3s and some of them were operating at GS-5 and 6 levels, and that was a continuing battle. It went on for more than a year or two before we got it finally resolved, not to everybody's satisfaction.

At the same time, we were trying to restructure the review. We created positions for medical officers called group leaders. We created review groups in the divisions, because the Division of Cardio Renal Drug Products had several different groups – it had a cardiovascular group, it had a GI group, and it had a blood group. We were creating these positions of group leaders, which were not supervisory positions. And as we were looking at who we were putting into group leaders, inadvertently, one physician, who had been a supervisory medical officer, was put onto a group leader position description, and the fact that he had been supervisory before, was missed.

Well, I was the guy who signed the SF52s, so he complained that I unfairly and in an unwarranted way, without any notice or rights, took away his status as a supervisory medical officer. That fact that it was a sheer oversight and literally a clerical error in personnel. Nobody would believe at all. “This is what you people in the Bureau of Drugs have been doing time and time again. You’ve been screwing your people.” I wound up being one of the people being investigated for that.

SJ: Well, the Bureau of Drugs did have a horrible problem with morale and perceptions. There is no sense of teamwork, or whatever it takes to get a job done.

JH: That’s one of the reasons Dick Crout was brought in, to try to do something about that.

SJ: Yes.

JH: I'll give you two other cases in point, because I think that the system was at fault and not the leadership of the Bureau of Drugs. The system included especially the personnel people and the legal people. There was never any way to get rid of somebody. Those examples are in addition to all of these people who were the subject of the Dorsen Report who should have been dealt with in a much more aggressive way.

There was a physician in one of the divisions – and I'm not going to use his name, but I do know him – who was a known and notorious alcoholic. This was a guy who routinely went out for a three-to-five martini lunch, who not only couldn't do any work but nobody wanted him to, because everybody was afraid of what he would do if he was trying to review something. So he would spend the mornings in his office reading the newspaper and the afternoon, when he finally got back from lunch, sleeping.

When I came to that job, working for Marion Finkel, I tried to do something about that. I said, "What's the record on this guy?" They brought out a pile of paper this big, and I was sitting there with personnel guys. I said, "This isn't enough?" "No, it's not enough, because, well, some of it's too old." I said, "Well, how long has this been going on?" "Oh, it's been going on for years. Some of its too old, it's not right. We can't..." I said, "Why can't we fire him?" "Well, he's an alcoholic, and you know, alcoholism is a disease." I said, "Yes, but if you don't agree to go through the treatment program, you can be dismissed. There are ways of doing this." "No way we can do it."

I said, "Look, what you're saying is there's no will to try to deal aggressively with this." And then I don't know if this was apocryphal or if it was true, but it was the rumor that was, "Well, his brother plays cards with Senator So-and-so every night or every week, and we can't rock the boat." It could be sheer rumor, but I heard it more than once. I heard it from more than

one person. So I said, “What you’re saying is, ‘Well, we’ll just give the guy a bottle and let him be happy.’” The man died of acute alcoholism or chronic alcoholism about a year later. So he resolved our problem.

There was another physician, who was a Commissioned Corps Officer, who was also reputed to be an alcoholic. Also one who was not very bright, not a good scientist or a reviewer. One who had gotten into some trouble for accosting a female pharmacologist. He was also someone who was just not somebody who was part of the solution; he was part of the problem.

They started the physician’s bonus program. Any medical officer who was a reviewer could get a bonus because he was an MD in a critical position. All of those bonus papers came to me to sign. I had to approve them, and I wouldn’t sign his. And I wound up in a giant-size fight with the Commissioned Personnel Operations Office saying, “I don’t want to put a premium on his retention. I want to fire him. I want a court marshal of him. I want to get him out.” And to make a very long story short, I said, “If you want to pay him a bonus, you find somebody else to sign the paper. I will not sign it, and I don’t give a damn what you’re trying to do, but I’m not going to sign it, and there’s no way you can make me sign it. And number two, I think we ought to be doing just the opposite. I think we ought to be doing everything possible to get rid of him.” He had eighteen and a half years in the Corps. After a long set of discussions, what was decided was let him work until he got to be twenty years and then involuntarily retire him so that he could get his retirement, and that’s exactly what happened.

Bureau of Drugs was not totally without... People didn’t have halos. Dick and Marion and Carl Leventhal and I, we’re all human beings, and I put my pants on one leg at a time and I didn’t have a halo and wings, and neither did they, but I think that we were basically honest people trying to do a good job in a system that really prevented it. I think that Dick and Marion,

who both received letters of admonition, and Merle Gibson and Bill D'Agvano, who also received some kind of letters, were scapegoats for a much more pervasive inability in the system to deal equitably with poor performance. Unless that's been changed a lot, I don't think it's any different right now.

I've been out of the agency for seven years, but I know that when I left in 1983, I didn't see any more enlightened administration in terms of personnel's ability to deal with poor-performing employees. I don't know that it was all their fault, and I don't think that I want to blame them. I think they were caught up in this same god-awful, slow-moving bureaucracy where nobody was willing to step forward and say, "Yes, do this," because there was always somebody who could say "no," and any "no" could stop any action. But every cog had to say yes before something would happen. It's like an electrical circuit: one open switch and the current doesn't flow; they've all got to be closed for the current to flow. I hope it's better. I can tell you that part of the generic system right now suggests that errors of the past 1980 suggest that they weren't very much better. Maybe for somewhat different reasons, but I have my own feelings about the generic situation. Yogi Bera would say 1989 was déjà vu all over again.

Back in the same generation of early 1974 period, or maybe it was late '74, the beginning of the bioresearch monitoring era. In retrospect, I guess that was the most celebrated case of fraud that FDA had. It wasn't played up that way, but it was the findings of discrepancies in reports of toxicology studies conducted by G. D. Searle that led to an enormous intensive investigation of Searle's toxicology laboratory, toxicology program, and many of their studies.

One lesson that one learns very quickly at FDA is that things can look too good. People who aren't thinking very well about how they want to fudge data, if they intend to fudge data, usually make it look too good. And the trained eye, somebody with a good biological

background, knows that biological variation in human and any kind of animal system suggests that the world is more random than orderly, and that blood pressures don't always change by two millimeters of mercury, or things don't always change in nice even increments, or the trend doesn't always go up when you think it should go up and always down when you think it should go down – there's always some scatter, some points that wind up in left field, that are just totally unexplainable, but they're real. When reviewers see these things they understand it; but when a reviewer sees something that looks just too good, he or she says, "Oh, I'm from Missouri. Prove it. Show me. Not so."

That's what it was when some toxicologists and pharmacologists at the Bureau of Drugs, reviewing some Searle studies in rodents, said, "It just doesn't look right." And that led to an investigation, where an investigator went out and did an on-site inspection, and came back and said, "It really doesn't look right, and it looks pretty bad."

The Commissioner at that point, when serious questioning was being called – with regard to these studies, decided to put together a task force. The task force had two components. The first component was a headquarters directive group. It was chaired by Carl Sharp, a Compliance Officer. The four people who were the nucleus of the headquarters component were Carl Sharp, Bill D'Aguano, who was the Chief Pharmacologist; Merv Shumate, who was the chief compliance guy for the Office of Compliance in the Commissioner's office; and me.

Then there was a field component. I don't remember the name of the man – I think he came out of New Jersey, he was one of the older, most experienced investigators. He led the field investigation, which involved many, many people, with on-site investigations and on-site data audits of every toxicology study that came out of that laboratory. What we found was basically that some things were done very sloppily, too sloppily: how they took care of their data

and the study materials. Some things were done fraudulently. It was written in, but it wasn't done or it wasn't done in that way. And there were serious indications that some findings that should have been reported to FDA were not.

The investigation went on for months, and box loads of data were brought in and they focused on individual studies with team of pharmacologists and investigators going over it study by study. This is the evidence gathering part, and things that the FDA in the field does very well. At the point; when they had enough real evidence to start writing a report, we presented this to the Commissioner at a staff meeting.

Schmidt directed that the four of us, who were the nucleus group, go sit in some vacant offices over in Chapman building. They would provide secretarial help when we needed it. But we were to do nothing else for as long as it took to get this report done, summarizing all of the evidence and making whatever conclusions that we could draw out of it. So Carl and Merv and Dag and I spent about four weeks there, and finally came out with a report. Much of what has been turned up looked bad but wasn't so bad, and a lot of stuff they'd turned up was terrible. In our report we reached the conclusions that there were some serious problems and presented that to the Commissioner. We also reached the conclusion that there were some violations of the FD&C Act, and that the matter should be referred to the United States attorney for prosecution.

Some of the people who were not involved on a day-to-day basis but who were very, very important in that investigation were Alvin Gottlieb, who at that time was Deputy Chief Counsel; Adrian Gross, who was a Ph.D. toxicologist/pathologist at that time working for Frances Kelsey, one of the people who found all this stuff. He was a headquarters guy who did the field investigations of these kinds of studies. The mad Hungarian. He was the one who filed a lot of

this stuff. Adrian could find sin, but he couldn't write it up in a way that made it useful in terms of remedial actions. They were very key players.

We had lots of meetings at headquarters and lots of meetings with the people who came in from the field, individual investigators that would debrief us on studies. We had one week where we were all out there in a hotel near Skokie, Illinois, on-site, right towards the end of this thing all of us were out there. Then when we came back and the Commissioner told us to go lock ourselves away; we did that. Every day the four of us met at 8:00 in the morning, worked until about 6:00 at night. I remember every day my wife would bake something that I would bring in. We had to do something to keep our spirits up, because literally, we were in a couple of big empty offices with four straight-back chairs and a couple of tables and boxes full of stuff. We'd talk about what we were seeing, what this all meant, and then I would dictate it and we'd have somebody transcribe it, and we'd start working from there.

I remember the final report was typed by two of the secretaries in my office at about midnight, and they misspelled assiduously. It came out assiduously. They missed it. And that report has a [sic] in it, you know, the [s-i-c], a misspelled word. That was the one line that kept getting quoted with the damn [sic] in it.

We had to make our presentation to the Commissioner at 8:00 in the morning and at 3:00 A.M., we were chasing around the Parklawn building trying to find an operating xerox machine to make the copies. One after another was broken down. We finally got it all done, we assembled it by hand, and the next morning at 8:00 we had enough copies to hand out to the Commissioner and the staff. They focused on the executive summary, and I remember Mac Schmidt sitting there – we're down at one end of the table and he's up at the other end. Peter Hutt, or somebody, said, "What do think about this?" He said "The hairs are standing up on the

back of my neck. I hate it.” “Well, do you agree with it?” And he said, “It’s not a question of whether I agree with it. Those four people down at the end of this table who wrote it, they believe it’s right, and I believe that they did an honest job of reporting what they saw, and these are their conclusions. It’s up to us to decide whether we concur with that as a group, and what we do with it.” He said, “But there will be not one word changed in this report. This report stands as it is. I may not like some of things I’ve read. I may have written it differently, but by God, that report stays as it is.”

I really admired him for that. It was one time when there was the Commissioner backing the guy seventy-seven layers down. He may not like exactly how we wrote some things and he may not have agreed with it; he may have felt that we overstated some things, but by God, the process was an honorable one. He gave us a charge, we fulfilled the charge, and there it was, and it was going to stay that way.

That led to a recommendation for prosecution, and a lot of changes happened. There are several. A lot of people got fired, and a lot of things happened. After many, many years, the U.S. attorney in Illinois declined to prosecute, which made a lot of people very unhappy. One of the people in the U.S. Attorney’s office later became a corporate counsel for Searle. We often wondered whether there was any hanky-panky on that end, but we all felt that that was not an appropriate things for us to think about. People can reach different conclusions about the strength of the evidence in terms of the ability to put somebody in jail. Our job wasn’t putting them in jail; our job was to investigate and to write the report. We did what we had to do.

SJ: Was it problems that was extending into their, any particular drug that alerted you? Were there any evidences that safety had been compromised?

JH: No, no, we didn't think so, because there was a lot of clinical evidence, too. The drug Flagyl I think was one of them.

JS: But said there were elements of the 1938 Act that they had violated. Can you be more specific?

JH: False reporting. It wasn't the 1938 Act, it was Title 18 of the Federal Code. False reports to the government. That's what they were in violation of.

That was a major revelation for FDA: The first time FDA really got involved in that level of review of toxicology studies. At another one of the hearings before Senator Kennedy, the question that was raised was, "If you found this with one company, what about others?" And that led to a further investigation of toxicology studies, and two others came out.

But the real bombshell was Industrial Biotest (Laboratories) in Chicago. That was another one where the Commissioner put together a task force, and I chaired that task force. This time I chaired and Carl Sharp was my right hand guy, and we had a lot of the same cast of characters from the earlier work, and again more field investigators. Here was, again, a blatant case of fraud where these studies were done in such a poor way that (a) in some instances they had no idea what really happened, and (b) they misrepresented the facts in what they reported to FDA. So it was another Title 18 case. That led to another report and led to prosecutions. This time there were prosecutions and some folks went to jail.

JS: Now, these reports that you're talking about, what happened with those?

JH: Oh, they exist.

JS: Do you have any idea where they might be? Do you know?

SJ: We can get them.

JS: Okay.

JH: Yes, go talk to Frances Kelsey. I'm sure that her office will have them because they came out of that division. I don't know if I still have my own personal copy of my Searle investigation report. I might have packed that away as a memento, but I haven't seen it in a while if I have.

[BREAK]

JH: Okay, you asked whether Aspartame was one of the substances involved in the Searle investigation, and it was. That brought in another wrinkle. We went out there, investigating not only drugs; we were investigating Aspartame almost from the beginning because it was so important. Here was a major sweetener that everybody knew if it got out there the exposure would be enormous. And I think that it was one of the causes of some friction between the Bureau of Drugs and the Bureau of Foods, because some of the people in the Bureau of Foods

really did not believe that the findings that the investigators were turning up were really significant in terms of meaning.

I'm glad you reminded me of that, because one day as we were writing the Searle investigation report, Dick Ronk came up to that room that we were in and was talking to us for a while. He was not a great believer in the validity of this report and felt that we were probably overstating the significance of these discrepancies with regard to the Aspartame case. And indeed, he may have been right. I'm not a toxicologist. I can't judge that. And eventually Aspartame was shown to be safe. We were calling them like we saw them. If the rat had a tumor, the rat had a tumor. If we didn't think the rat had a tumor, the rat didn't have a tumor. We had consultant pathologists looking at slides as part of this investigation on a number of different substances. But they were contemporaneous in time, the Aspartame with the drugs. Aspartame was clearly one of the substances we were investigating. It was one of major public interest, and one that did lead to some mild friction between the Bureau of Foods and the Bureau of Drugs; nothing lasting.

SJ: We also have a note to talk about Three Mile Island. I know FDA's role in that was somewhat peripheral.

JH: Yes, I don't know that FDA's role as peripheral as you think. I think FDA's role as pretty important.

SJ: Oh, good. Well, tell us.

JH: I will tell you about one part of it only. But you've got to talk to John Villforth, because John Villforth was "our man" for Three Mile Island, and he was the FDA official most directly responsible in a broad radiation public protection situation. I was involved because of one aspect of it only. It's funny, I just wrote a paper on this, and I'm still a little fuzzy. I gave you a copy of that paper, didn't I? I'm a little fuzzy on exactly when it all started. It was in March of 1979. I remember that there was an accident at Three Mile Island and a potential release of radioactivity. I had been involved with the National Council of Radiation Protection and Measurements (NCRP), as a consultant to their Report #51 on radiation protection and the thyroid gland in terms of nuclear emergencies. When this Three Mile Island situation came about, the question was raised, "What's the potential for thyroid exposure, and should we be thinking of potassium iodide?" I got involved in that discussion. The question was, "Were supplies available?" At the time this came up it was still early. Nothing had been released. Nobody knew how significant this potential for a release was and whether we were going to have a catastrophe on our hands or not.

Well, we started making some phone calls about the availability of potassium iodide for thyroid blocking. There were no tablets of the right size available. All the tablets were 300 milligrams which were a dose used when potassium iodide was used for asthma as a bronchial dilator something to increase the flow of mucous. It was an expectorant dose, which has been shown no longer to be a safe or effective dose. The 100 milligrams that we needed for thyroid blocking didn't exist in tablet form, so we started calling around the drug companies that marketed potassium iodide solution, or saturated solution of potassium iodide. Did they have any on hand and if so, how much? And what we were looking for was a quarter of a million bottles of it, or enough to protect a million people, because there were a million people in the

metropolitan Harrisburg area. Nobody had anything like that capability. You could buy of a couple of dozen bottles at a time.

Somebody thought, well, we could make this stuff before they started thinking, how much are we talking about here? There were several of us who got involved. After I was told of this, I made several phone calls. I asked Bob Frankel, who used to be another pharmacist, Rad. Health certified health physicist, pharmacist who came into the Bureau of Drugs. (He filled the job that I had had working with Marion Finkel when I became Deputy Director of the Bureau.) And Paula Botstein, who is there now as a physician. And the three of us got together talking about this. I had been involved in helping with some guidelines on potassium iodide that were starting to be thought about, but nothing was really ever done with that at that time. So we sat down with pencil and paper and figured out that what we needed was sixteen thousand pounds of potassium iodide, or eight tons of potassium iodide, put into solution, put into bottles. You can't get that from drug stores in one week. You can't get that from a pharmaceutical manufacturer. Nobody's got that much around.

We started thinking, "Well, if we need this stuff, we're going to have to get somebody who's a chemical supplier." And we called Mallinckrodt, and found out that, yes, Mallinckrodt has large amounts of potassium iodide crystals. So when we could locate the supply, hours had since gone by and I talked to John Villforth again, and I said, "Well, what's the status? Do you want me to try to get this stuff put together into solution and get it ready for use?" He said, "Yes, I think you better." I said, "Okay." Now this was I think a Friday night.

JS: The potassium iodide that you were going to get from Mallinckrodt was this a USP preparation or was this a chemical?

JH: It was both. What we started out with was potassium iodide crystals made into, at my direction, saturated solution potassium iodide USP, or potassium iodide solution USP.

I can't remember exactly the scenario here, but it was late Friday night, and I called Mallinckrodt in St. Louis and I got a hold of a security guard and I identified myself, and I said, "I've got to talk to somebody in charge. How about your radiation safety officer or your plant safety manager or what have you?" He got me that person, and had them call me back. I identified myself and told him what the issue was and he said, "I can't make that decision. Let me have our vice president call you." I said, "Okay, but do it fast." So I got a call from the vice president and I started in again, and I told him what we needed. I said, "I want 250,000 ounces of potassium iodide solution." And I said, "Right away." So he just kind of gulped and said, "I'll call you right back."

He called back in a couple of minutes, and said, "Okay, what we can do, we've got enough of the chemical, and we have a plant in Decatur (Illinois). The chemical's in St. Louis. We've got a plant in Decatur that we can truck this stuff up to and we can start putting it into solution. But I don't know that we've got enough bottles. What do you want?" I said, "We want one ounce dropper bottles." He said, "I'll have to call you back." I said, "Okay. In the meantime, get things moving." So later on that night he called back and said, "The only thing we have are square one ounce powder jars. Some of them have metal caps. "This won't pass good manufacturing practices (GMP)." I said, "I don't care." He said, "They don't have droppers." I said, "Well, get droppers." I said, "Do you normally have dropper bottles?" He said, "Yes." I said, "Who do you get your droppers from?" "There's an outfit in a little town in

southern New Jersey.” I said, “Okay, you start going. Call me when you’ve got the first lot ready to go and we’ll make arrangements for transportation.”

In the meantime – I didn’t know how long this was going to be – I went home and I went to bed. I’d left my phone number here at the Emergency Epidemiology Operations Group, Dick Swanson’s group. They got the call, they relayed it to me, and at 2:00 in the morning he called me and said, “Okay, we’re ready to go. What do we put on the label?” I remember sitting in my bed and at 2:00 in the morning dictating what the label would be. He said, “What kind of a label is that?” I said, “That’s the label. I will take full responsibility for it. Just make sure it’s the USP Potassium Iodide Oral Solution (SSKI), put some potassium thiosulfate in it, which is one of the preservatives in it, and we’ll not worry about the GMPs or the fact that the labels aren’t going to be printed with lot numbers and all that other stuff.” He said, “Well, we’ve got some little hand machine; we can crank out the labels at this hour of the night.” I said, “Run it on the hand machine. I don’t care.”

They called me back about four hours later. By this time I had gotten dressed and went back into the office. They had the first batch of approximately thirteen thousand bottles. I had by this time called the Dougherty Brothers Group in southern New Jersey and said, “I understand you guys make droppers.” “Yep.” I said, “I want a quarter of a million of them.”

JS: (Laughter)

JH: He said, “I don’t have a quarter of a million in one size.” I said, “I don’t care. I want a quarter of million of them.” He said, “When? How?” I said, “I don’t know. I’ll call you back. I’ll let you know. Just get a quarter of a million droppers put together now.”

I called a coordinating phone number in the government and I said, "I've got to arrange air transportation and truck transportation." They patched me through to somebody in the Pentagon, in the Air Force, and I said, "I need an airlift." He said, "Who are you and what..." So I told him who I was and what I was doing. He said, "What do you want?" I said, "I need an airplane from your base in Illinois near Decatur to fly potassium iodide to Harrisburg, Pennsylvania." He said, "Are you crazy?" I said, "No." And he said, "Well, hold on." He had me hanging on for about ten minutes. He came back and he said, "What's your account number and what's your..." I said, "Look, man, I've just bought 250,000 bottles worth of this stuff and 250,000 droppers and I don't have any purchase order. I don't have an account. I've got a nuclear reactor that may be going to go apart and I need this stuff moved." He said, "Okay. All right, we'll take care of it."

We had an Air Force plane get the first load of this stuff, put up in the wrong kind of bottle. The labels weren't even on – they were shipped with it – with no droppers. I got somebody in the Pentagon who patched into Fort Dixon, New Jersey and we got an army truck to go down to this Dougherty Brothers place, and they loaded up one of these big army trucks full of droppers and they hauled them to Harrisburg. And then we realized, "Where in the hell are we taking them to Harrisburg?" We just realized we had nowhere to put it. So I called John Villforth and I said, "Hey, John, we've got a plane coming in with bottles and I've got a truck coming in with droppers; where does it go?" It was only then that we remembered we hadn't told the state. So they started quickly scurrying around, calling the state health officer, and everybody concerned.

Everybody got patched in and the state made a warehouse available. We made arrangements for the state to have a truck at the airport to pick up the stuff from the Air Force

plane and bring it in to the warehouse. The next call from Decatur told us, “Look, we can’t go fast enough. We’re never going to get this stuff done for you fast enough. We’ve got to get somebody else to bottle. We found out that Parke-Davis in Detroit can put this stuff in bottles if we can get them the saturated solution of potassium iodide.” He gave me the name of somebody in Parke-Davis.

I called that person. He said, “Yes, the people from Mallinckrodt have called us, but we’ve got some real problems here. Number one, we don’t have the right size bottle.” I said, “What have you got?” He said, “We’ve got two-ounce dropper bottles.” I said, “Great, we’re going to fill those half full.” “Wait, you can’t do that!” “That’s what we’re going to do.” He said, “Well, what will we put on the label?” I said, “You put the Mallinckrodt label.” “We’re not putting Mallinckrodt’s label on it!” I said, “That’s what you’re putting on it. You don’t have time to reprint your own label do you?” He said, “No.” I said, “Neither do we. Do it.” He said, “Well, I’ll tell you, the only way we’re going to do this is, if there’s an FDA man standing right there watching this so we don’t get in trouble afterwards.” I said, “Sold.”

I got a hold of either Paul Hile or Don Healton. One of those people. I told them what I needed. They got on the phone and they called Al Hoeting and Al Hoeting the next day was standing there in the Parke-Davis plant telling them, “It’s okay, you can do this.” The Air Force then balked. The Air Force would not take the next shipment because I didn’t have an account number, and nobody knew what the hell an account number was and didn’t know where to get it.

So I told the people at Mallinckrodt, “Charter an airplane.” The guy said, “On your say-so?” I said, “You betcha.” “Okay.” I told the people in Detroit the same thing: “Charter airplanes.” So by Tuesday or Wednesday, we had 239,000 bottles from Decatur and from Detroit on-site in Harrisburg. During this time, we had found out that the state of Pennsylvania

had their state pharmacist look at this stuff, and was damn concerned. Number one, he found something that was really very important. He found out that the dose was wrong, because the USP dropper is calibrated with water and the number of drops per milliliter is based upon the size of the drop with water. Nobody had even thought of the fact that the specific gravity is so much different with this stuff that the number of drops is different, because the surface tensions are different with this saturated solution. It's heavier. The drop falls off faster. He said, "Well, you're going to under dose or the people are going to give the wrong...or the label's wrong. One or the other."

We had a meeting with the MDs. Bill Stead and Botstein were both involved in that. We figured that there was enough leeway in the dose that if they under dosed a little bit, it wouldn't be bad. We said, "Okay, stick with what the number of drops on the label is. They'll get a little bit less, but it's okay. They're supposed to get 130 milligrams of potassium iodide; they'll get a little less than that. It's still enough for a thyroid blocking if you've got to use it." "Well, all right." "The labels aren't on the bottles." I said, "Yes, with the first batch. They're in the box. If you have to use them, somebody's got to lick them and put them on." "There are no droppers." I said, "Yes, they're there. They go along with it. They're not dropper bottles unless you got the batches from Detroit, and then the bottles are only half full." He said, "What kind of rinky-dink operation is this?" I said, "It's literally the fly-by-night pharmaceutical company making potassium iodide on a moment's notice." (Laughter)

End of story was, thank God, they didn't have to use it. And then we had the problem of what do we do with it?

SJ: What was the total bill on this? Did you add it up? (Laughter)

JH: Oh, I'll come back to that. Because there's a good story that goes with that. When it was all done, what are we going to do with it? I said, "Destroy it. This stuff is absolutely in noncompliance with anything. We didn't need it for an emergency, get rid of it." "No, no, now that we've got it we've got to do something with it." The decision was to get it all down at Arkansas, and they hauled it all down to National Center for Toxicology Research (NCTR). And every six months I would get samples and I would send them over to Bureau of Drugs lab and we would assay them.

The people down at Arkansas would look at the bottles. After a year or two, they said, "Look, the ones with the metal caps are really corroding." I said, "Destroy them." "Well, we can't do that because EDRO is controlling these things now." I said, "Fine." I went to Paul Hile, and said, "You'd better get the order down there to destroy them." He said, "Fine." So we got rid of those, and they kept others that were in the plastic tops and the ones that were in the dropper bottles for years. That was the only national supply until we got to the point where the assay dropped below USP potency levels because the stuff got so old, or they were just tired of looking at them. Then they finally got rid of them.

Now, you asked me how much it cost. I never knew until the day I retired. All I knew was the guys from purchasing came to me the Monday morning after all this started and said, "Why didn't you get a number?" I said, "He's asking me for a number. How the hell do I get a number?" He said, "We go through this all the time. Somebody should have called you. There's one guy who could just give you a purchase order number over the phone and you could use that for everything." I said, "Well, I'm sorry. I didn't know that." Right then and there we made a new Standard Operating Procedure (SOP) in case we'd have to do this again. The day I

retired I was presented a certificate, one of the ha-ha's at my retirement, for the largest unauthorized purchase in the history of the Department of Health, Education, and Welfare (DHEW). One hundred and forty thousand dollars is what the bill was, and I think that some of the people never charged for the stuff. I don't think that Mallinckrodt ever submitted a bill. I think that this was the airplane charters and some of the other stuff. We wound up giving Commissioner's Special Citations to Mallinckrodt and Parke-Davis and for those of us who worked on it. It was, in retrospect, a lot of fun. It was an example of what you could do if you really had to. And thank God we didn't have to use it.

But I think I told you when we met the last time that in 1988, I was asked if I would speak about Three Mile Island when we had the International Pharmaceutical Federation meeting in Australia. I said, "Well, the panel is about the role of a pharmacist in emergency situations, and that's a good one." I said, "Okay, but it really is out of date." I was reminded, "Yes, but the tenth anniversary's coming up." I said, "Okay." I said I would do that on the condition that I update it with Chernobyl (USSR).

I wrote the paper and I got the Department of Energy reports on Chernobyl, and I saw that they used potassium iodide in Chernobyl. I then went back and made the same phone calls to all the companies I had called years before asking if they had any stuff on hand. Now, in the ensuing time some NDAs had been approved for potassium iodide tablets, 1—milligram. Nobody kept any on hand. Most of the states don't require it. The federal government specifically doesn't require it and doesn't endorse it on the basis of cost benefit. They don't think that it's useful. And the conclusions in my paper were that if Three Mile Island happened today, we'd do it all over again the exact same way, because we are as unprepared today as we were in 1979.

It's interesting. I have gotten more reprint requests for that paper than almost any I've ever written, and all but one of the reprint requests were from Eastern Europe, except one from a physician at Cornell who is an active member of the American Thyroid Association, who read it and said, "The American Thyroid Association agrees with your position." At one time they didn't. They didn't think that potassium iodide was necessary or desirable for thyroid blocking. And it was kind of interesting to see that the world's turned around.

SJ: Do you have any idea how the Soviet Union handled getting their supplies cyclically? They would be in much better shape than we were.

JH: It was stockpiled.

SJ: It was stockpiles. They already had it. I was going to say, because...

JH: They only had, in the village of Pripjat, (USSR), near Keiv and near Chernobyl, about 135,000 people total, and they all got it within twenty-four hours. It was used, and they kept the radiation doses to the thyroid fairly in line compared with what they could have been. Lots of people got some zapped doses from Chernobyl, but the general population at least was spared thyroid doses.

JS: Are there any bottles left? I mean, I would love to have some of these for our collection. But apparently, everything was destroyed, right?

JH: I have private stock.

[BREAK]

JH: Okay, you were about to ask me if I would part with some of my collection, weren't you?

JS: Well...

JH: Well...I'll tell you what, you hold on to this, and at least let me see if I've got a picture over here. I don't know if any exist in the agency at all. I had hoped that people would have kept a few for just that reason, for historic significance. That's one of the reasons I gloomed onto six of them, so I will be happy to donate them to historians.

JS: Well, you were going to begin telling us a little bit about the bioresearch monitoring at FDA.

JH: Okay. I don't remember whether it was 1974 or '75. I tend to think it probably started in late '74, because it was shortly after I arrived at FDA, and I was working for Marion Finkel in New Drug Evaluation. The issue in those days that really served as a springboard for later, large program related to what later turned out to be incredibly mismanaged and in some areas falsified toxicology studies conducted by Searle in Skokie, Illinois. And these were found by toxicologists, FDA's pharmacologists who were reviewing the studies and it didn't look right, just didn't look right. When a study doesn't look right, it's basically because things look too

good. There's not enough random biological variation, which is the way that biological systems really behave. Blood pressures might – the analogy is one in the clinical area, but it would hold the analogy to an animal area – blood pressures may change by too regular an interval. It doesn't happen normally. Blood pressures fluctuate around. Clinical chemistries, the values may change, they increase or decrease by the same decrement over time – it doesn't happen that way. Biological systems are more random. They vary.

So the toxicologists who were looking at these studies in FDA said, "It doesn't feel right; it doesn't look right." And they asked for the studies to be audited. And that assignment went to Frances Kelsey's division. Kelsey was then...Not even a division, I guess, it was a...It wasn't even called Bioresearch Monitoring. It was called the Clinical Investigations Staff, and it was a staff function in the Office of New Drug Evaluation. It had only a very few people working for them. Dr. Kelsey, who is an institution unto herself, and if you have not interviewed her for your oral history you are missing somebody.

JS: She has been.

JH: Good. Alan Lisook, and there's one Consumer Safety Officer in there whose name I have forgotten. At that time I think we had just put Dr. Adrian Gross into that division. Dr. Gross was a veterinarian who had kind of a checkered history in the organization. Just one of these people who is so charming and so much fun – a little on the coarse side, but charming and a lot of fun. The mad Hungarian. I don't know if he was Hungarian, but he was from Europe originally, and he spoke with an accent, and we used to call him a Hungarian. But he just wasn't interested in just sitting down and reviewing data. He liked to do other things, and he had an

uncanny knack for being able to ferret out inconsistencies and problems. And Gross went out with an investigator.

I guess first it was an investigation from the district office in Chicago, and the investigation report came back and the investigator said, “This is a little above my head. I could really use some help here, because I can’t interpret some of the things I see.” So we turned it into a deeper investigation and Dr. Gross went out with the Chicago district office investigator again. He came back and his initial findings were that there are very serious problems in the toxicology department at Searle and that it appeared that the studies just were not valid because of what he saw in research records, things that he didn’t see that he felt that he should have seen, and the general chaos. He felt that those studies just could not support the conclusions that were there attesting to the safety of the drugs.

It’s sixteen years, or fifteen and a half, and my memory’s kind of hazy, but at some point shortly thereafter, this became...it went right up to the Commissioner’s office. It was just no (Inaudible). It seemed to be so serious because it involved a major drug company and it would clearly have a major impact on whether their applications were going to be approvable.

JS: Applications for...

JH: NDAs, for new drugs.

JS: Which drugs in particular are we talking about?

JH: I really don't even remember. I honestly don't remember which drugs they were. It is comes, I'll tell you, but right now I don't remember. But the Commissioner was Dr...

[BREAK]

JH: All right, the Commissioner, who was Mac Schmidt at the time, created a task force that reported directly to him. Carl Sharp, Carlton Sharp, who was a Compliance Officer in the old Bureau of Drugs, was appointed the chairman. Carl was one of those very unique, non-supervisory GS 14s who had a great deal of independent authorities because of his knowledge, his experience, and his stature in the organization. He was one of about three or four people who had a unique staff that reported to Ted Byers, who was the head of Compliance. He was Dan Michels predecessor.

A number of people were put on the task force. I was put on the task force from the NDE Office. Dr. William D'Aguano, who was the Chief Toxicologist also in the same office, was put on. "Dag" as he was called was the real scientist in the group. Mervin Shumate, who was in the compliance group, worked for Paul Hile in the Associate Commissioner for Regulatory Affairs office, was on it. And we were the nucleus. The four of us were the nucleus, and then there were a lot of other people involved, including Al Gottlieb, who was at that time Deputy Chief Counsel. There was another counsel, a woman who had been a...Joann, Joann, can't come up with her last name. First name was Joann. She had been around for a number of years and a very experienced counsel; she was on it. Dr. Kelsey was on it; Dr. Gross was kind of consultant to it. There were some pharmacologists from the divisions where they were reviewing these documents, and a few other people.

It was our job to organize how we were going to look into this, identify what the studies were. And the decision was made not only to look in depth at the studies on the drugs that we knew about, but to go back and look at other Searle drugs and do an in-depth review of the pharmacology studies in the files already, some of which may have been reviewed before and accepted. On the basis of that review, a number of other studies were identified for on-site data audits – going right to Searle and looking at the original research records for these studies. It became apparent that an on-site effort involving a number of people was going to be necessary. Another component of the task force was created, and this was the investigative arm of it. I can't remember who the Chief Investigator was? He was a very, very senior fellow from Philadelphia. We called him the colonel, because he had been in the military a long time.

JS: He was an actual colonel then, not an auctioneer colonel?

JH: No, he was an ex-military guy. I don't know if he was the colonel, but at the end of the whole thing when we had a big celebration a long time afterwards, Adrian Gross wrote a little parody about the colonel. But he headed up an investigation staff that included a lot of investigators from all over the country who were detailed to this job. And they set up headquarters in a motel; I think it was in Park Ridge, Illinois, which isn't very far from Skokie. Over a period of months they spent hour after hour every day in that laboratory pouring over records. And things got a lot worse before they got better, because they really found that there were some studies that were just, we believe they were fraud. We believe that there were other studies that were just so poorly done that there was no way you could understand how they reached the conclusions that they did about the outcome of safety.

JS: Were these studies actually done in-house or had they contracted these out?

JH: They were done primarily in-house. A few had been contracted out to Hazelton Laboratories, but most of them were in-house. For those that were done in Hazelton, we identified those that he wanted to look at, and we sent the notice to Hazelton and they looked at the studies that were done at Hazelton. The Hazelton studies had some problems, too. Not as bad in terms of the on-site handling of the animals and of the data, but in the report writing phase, who wrote what and then who edited it to say what and on what basis.

The field operations were completed after several months, and we got the inspectors' notes, and all of the official inspection reports, and then it was up to four of us – Sharp, D'Aguano, Shumate, and me – to write the report of the task force. And the four of us were detailed from our jobs and for one month we were put in some vacant offices over in the Chapman Avenue building and we poured over all this stuff and pulled together a report. And I think I told you about running around the Parklawn building literally at 2:00 in the morning looking for operating xerox machines and such to get the thing done to present it the next morning at the Policy Board. We did that.

The Commissioner was not very happy with our report. I don't know whether he believed things were as bad as we said they were or whether he just didn't want to believe that any company would screw up that badly. But he accepted the report and said that he may not agree with everything in it, but nobody's going to change anything. This is the report. This is what we're going to have to deal with, and it would then be turned over to the established compliance side for enforcement. What do we do about it? And it led to a grand jury in

Chicago. It led to years of preparing a case. And finally, it led to the U.S. Attorney in Chicago deciding he was not going to bring the case, which made a lot of us very, very unhappy. It made us unhappy when he went to work for Searle.

JS: What grounds? On what grounds did they...?

JH: The U.S. Attorney has the authority to decide whether the evidence is sufficient enough to bring a case.

JS: So that was the reasoning? No evidence, insufficient evidence?

JH: Yes. There are records of that. I think you ought to go talk to Carlton Sharp and find out why. Because Carl spent months in Chicago working with the U.S. Attorney's office and I think that the staff-level people were ready to go. And as I said, he later went to work for Searle.

JS: Searle counsel or some other position?

JH: As part of Searle's legal counsel. Or he went...Maybe he didn't go to work for Searle – I'm sorry – he may have gone to work for the law firm that Searle retained. So, I don't want to leave the impression that he did something that was illegal, but it was certainly, the appearance problem was certainly there. Because even if he went to work for the law firm that was representing Searle but never got involved in any of the business that affected Searle, the mere

appearance is that he left the position as U.S. Attorney after having declined prosecution and then went to work for the firm that was defending Searle on this issue's legal front.

JS: Was any of this publicized?

JH: Oh, yes. Oh, sure. There are public records on all of this.

JS: Newspaper, that sort of thing.

JH: Yes. And again, Carlton Sharp is the real resource. Well, Senator Kennedy held some hearings on that. This was great stuff. And this was one set of hearings where FDA was not raked over the coals. We were the guys in the white hats; we were okay. But as an outcome to that hearing, it was asked, "Gee, if things are so bad here, how do you know they're not this bad all over?" As a result of that, a concerted effort was made to look at other toxicology laboratories and other toxicology studies, and toxicology studies from other pending NDAs were reviewed and assignments sent out to the field and a lot of drug companies' toxicology labs were inspected and a lot of contract labs were inspected.

Out of that group, there were two very big cases: one was Biometric Testing Company in New Jersey. We used to call this the rubber rats case, because literally a number of studies' reports and records from on-site investigations were written – and again, ask Carl Sharp who was involved in this too; he was involved in all of these – it looked like they were the same rats, the same ones. If a rat died, they didn't record it as a death; they just put another rat in the cage with the same number. Now somebody went to jail as a result of that.

A much, much larger case came up a little later on. That was Industrial Biotest in Chicago. Again, a task force was created, and this time I was the chairman, and a lot of the same people worked on it. We did the exact same thing: on-site investigations, looking at the study. Here was a large contract laboratory and it was a disaster. I mean it was just an absolute mess. We wrote the report, submitted the report, the place literally was closed up, went out of business. I don't know if anybody went to jail, but there was a lot of enforcement action that came out of that. The worst of all of this was all of the time and money that the companies who had contracted with these laboratories had invested for their drugs was wasted, and they had to go back and repeat the studies before we'd be able to approve the NDAs. So it was very costly.

Now at the same time, the concern started to come up that periodically, FDA used to look at the clinical studies. This was what Dr. Lisook and Dr. Kelsey were experts at, and they would look at not only what the clinical investigator himself did, but what the drug company did in terms of monitoring, what the Institutional Review Board did. There weren't a lot of regulations in those days. What all of this grew out of, and it's important to recognize, it grew out of human rights violation. These grew out of the Nuremberg trials. The horrors that the Nazis perpetrated in the camps on people with human experimentation led to the Nuremberg trials, and the Helsinki agreements, and then the Tokyo agreements, so there were a series of international declarations about human rights in clinical research. Most of these were guidelines in the U.S. There really weren't a lot of regulation. Periodically, somebody would mention to Dr. Kelsey and Dr. Lisook: here's a clinical study that doesn't look quite right. Again, it was usually because it looked too good; the outcomes were just too favorable. They'd go out and they'd review the clinical data, and sometimes they'd go out with a field investigator. Occasionally, if they found that the trial was not right and the clinical investigator wasn't living up to what was

expected of him, it would lead to disqualification. Disqualification was a process, by which a clinical investigator was then prohibited from doing IND studies, and his name was published, available to the industry and he was blacklisted forever. There were a couple of cases where people appealed to try to get back in. If one appealed and enough time had gone by and people felt that he learned his lesson, they'd rescind the disqualification. This list is available today. It goes back to the first guy they ever disqualified back in the sixties, and let back in again. Most of the time, if somebody got disqualified, he was so scared to do this again, and he never wanted to return anyway.

But looking at the clinical side was increased renewal based upon what was found on the animal side, and sure enough things were as good as they should be. There were a couple of things that happened at that same time, like dimethyl sulfoxide (DMSO) studies, which led to a number of disqualifications of people because they were doing just absolutely poor work. It led to a lot of things. It led to me being investigated by the Inspector General and the U.S. Attorney of Baltimore.

Dick Crout and I were accused by one of our employees of refusing to prosecute certain physicians, and this was seen as a cover up to DMSO for some reason. Why anybody thought that we had any great feelings about DMSO I don't know. One of the physicians, at that time in Frances Kelsey's organization, was one of these people that if you didn't do it his way you were wrong. He was also one of these uncanny guys when it came to ferreting out the truth about the study. He could look at the documents and he could find out where the documents were either not done right or falsified. But he was also one of these people who saw things in blacks and whites; there were not grays. If it wasn't perfect, it was criminal. I've always felt that the world is made up of lots of shades of gray.

There were two cases in particular, involving DMSO investigators, where I just felt that the people were not really prepared to be clinical investigators. They were clinicians. They were treating their patients; they weren't doing clinical trials, and that disqualification was enough. They wouldn't do clinical research any more. But I sat at the table when we had a disqualification hearing; I was the disqualification official, and I met with two of them. These were both urologists, and I just could not make myself believe that these guys were crooks. They were just clinicians treating patients and they weren't well-informed by the sponsor of the drug as to what their obligations were, using this drug as a research tool. I disqualified them. They didn't like it, but they said, "Okay." But I would not agree to prosecute them.

When something like this happens, when you have a dissident employee, he goes right to the Hill or right to a reporter or right to somebody. I think he called a hotline. We had a hotline at that time, and we were being investigated; it went on for months and months. I had a number of visits by investigators. It might have been Senator Kennedy, but it went on a long time. The worst part about that was the ground rules were that during the period we were being investigated; neither Crout nor I could have direct communication with the Commissioner. Everything had to go through Nancy Buc, Chief Counsel or Paul Hile, Associate Commissioner for Regulatory Affairs, which we felt was just absolutely awful.

Jere Goyan was Commissioner at this time. So you could see a lot of time had gone. Mac Schmidt had left. This was the second half of the Carter administration by this time, so a lot of time's gone. We just felt that that was terrible; it was really unfair and it was really inhibiting to solving the problem. But neither Crout nor I was concerned about that. We knew that we would be vindicated through all this.

It turns out that one of the employees in the Bureau of Drugs took some payments from the major sponsor of DMSOs. It was Dr. Pani, an Indian doctor. A long tragic story. I wound up testifying for the government. I was the government's witness in the prosecution against Pani and against a Dr. Stanley Jacob, who was then the father of DMSO in Oregon. Jacob got off scot-free, which I thought was terrible, and poor Dr. Pani was kind of left holding the bag. He did not get a jail sentence. I think he got a suspended sentence, but he was certainly found guilty. It was really a mess. He was not a very bright guy, and his wife was dying of diabetes and had had a number of surgical amputations, and he needed money for medical bills. It was really a very, very unfortunate thing. He kind of got suckered into it, and I felt sorry for him, but he really should have known better than that.

JS: Why did Jacob get off scot-free?

JH: Beats me. I had testified against them, and he essentially turned around and pleaded guilty at the end and then nothing happened to him. They dismissed the charges against him. And I was furious with that. I felt that that was totally undeserving.

There were a number of clinical investigations that turned up problems, and more hearings in front of Senator Kennedy. The person there who was the star was Michael Hensley; he was the Adrian Gross of the clinical investigators. Both of these people were very good investigators, but again, they only saw black and white. And if they saw something that was not perfect they saw sin and they saw veniality and they saw criminality. They both loved to testify with all of the klieg lights and all of the...They were wonderful puppets for a Congressman or

Senator and his staff, because they would say anything and they didn't care whether it reflected badly on FDA or not. They were the pure.

As a result of all of that, we got the clinical investigators regulations moving along and the sponsor monitor regulations. Then what came out of those later on were the institutional review board (IRB) regulations and the bio availability laboratory regulations. It took a long time. Many of the regulations appeared in only, the good laboratory practice regulations (GLPs), which appeared in draft from in the seventies. Maybe the sponsor monitor regulations appeared right before the end of the decade. The others didn't even get into drafts until the eighties, and it wasn't until well into the eighties that they were finally made final regulations, because it was a long, difficult and complex process.

You walk a very fine line. FDA has enormous power, and it has to balance that power in a way that you don't want to stifle creativity and research. You don't want to create a cast of regulations that are so rigid that there is no opportunity for innovation and progress that you can't get better, you can only stay within this mold. And I thought that, in general, FDA did a very good job, probably as good as it could do, because when you looked at the comments that came back from the proposals, these were comments that reflected the biases of the industry on one side, the clinical investigative population on another, but then the advocate or the consumer activist on the third side, who was prepared to throw all these people in prison if somebody forgot to write down a blood pressure. In this I gave people like Hensley a lot of credit, because sometimes when I had a lot of trouble with him, it was because of his philosophies, not because of his knowledge. When you had people like Alan Lisook and Mike Hensley, who are both good physicians, go out and look at a clinical trial, look at the records, what are you going to find? Are you going to find that the nurse forgot to record a blood pressure? They forgot to administer

the drug one time? Did they administer it late? Or a procedure wasn't done exactly when and how it was supposed to be done? But that's life in a hospital. You try to do it perfectly, but boy, if you see a study where every dose is given and it's really given on time and every specimen is collected and every blood pressure is measured and even laboratory value is collected and is recorded in the record and all of the pieces of paper are together, boy that's remarkable, because it's hard to do. There are so many things that happen, so many parties involved when you're dealing with people in a health care facility who are both being treated and are the subjects of research, that it's tough. The average trial always has omissions and errors.

The trained physician who is looking at those records from the point of view of the investigator looks at that and says, "It's okay." Where you take the average non-physician investigator, who may be a terrific GMP investigator in a factory and ask him to do the same thing, he has a lot of trouble, because how can he live with this? Here are some records that aren't available. Here are some things that were missed. How does this equate to what the goals of the research are and the validity of the data being collected in that research. That's why having the physicians involved were very good. But at the same time, it really did make for a harder job. Not only writing the regulations, but defending the agency's position that you want to go far enough to reduce the probability of serious error, either omission or commission of some event as low as possible, but you don't want to go so far as to prevent physicians from being good investigators and being good physicians.

Same thing with the IRB regulations. You could build protections into the institutional review that stifle all research. Some of the institutional review boards I think, and I saw this in my industrial experience, were nuts. Even in enormous institutions.

As a digression, when I was with Ciba, we were doing a number of studies with a very old drug, phenylpropanolamine, but the fifth most common drug in terms of doses taken in the United States, or at least it was back in '83, early eighties – most of it because it aids in decongestion, a lot of it because of weight loss – we were doing studies of that drug at the University of California Medical Center at San Francisco, one of the leading medical centers in the United States. Their IRB finally said, “We don’t want this drug to be studied anymore. We have concluded that it’s ineffective.” “On what basis?” “Don’t know.” We objected to that, Ciba did, but moreover, the drug studies unit at the university just went up in arms, said, “That’s nonsense. That is not your role.”

[BREAK]

JH: The University of California IRB was rejecting study proposals for good studies that were intended to elucidate the truth about the drug. So here they had already made up their own mind that the drug was not worth it because it was ineffective – which was wrong. We went to other institutions and did efficacy studies and safety studies. But the point was that the IRB obscured its role. Its role was to protect people from unnecessary risk in clinical research involving drugs, and it was doing other things. It was making value judgments about whether anybody should get the drug or not. That wasn’t their job. Their job wasn’t even to look at the protocol from the point of view of scientific validity really. It was really to ask, are people protected? Are research subjects protected from unnecessary risk? Do they know their rights?

So in FDA’s evolution of the IRB regulations it had to contend with: the industry’s interests, the interests of the health care facilities where the research was being conducted and

wanted to limit their liability, the guidelines that the NIH was using, and the fact that NIH was also drafting IRB regulations for use there. And a lot of these things were very complex negotiations where on some of them it didn't matter if FDA and IRB were talking, and NIH were talking to one another. We didn't have all of the facts. We had to go outside and hold some public workshops and get some input.

It finally led to, I think, a remarkable series of regulations. Some of them, people will argue, have gone too far and they have increased the burden on researchers and on the industry substantially in terms of cost: in cost of record keeping, in cost of time. From all of that, I think that enough time has gone by now that industry has learned to live within these regulations, and the quality of clinical research and the quality of all bio research in the U.S. has improved.

What the U.S. did was a template for the world, because you see very clearly evidence of the dispersion of the U.S. regulations throughout the world, mostly the non-clinical laboratory regulations, good laboratory practice regulations. And indeed, other countries jumped on that bandwagon because FDA said that it would conduct audits of certain, toxicology studies in other countries that were submitted to the FDA in NDAs from U.S. companies. When FDA started sending inspectors to Switzerland and England and Sweden and other countries saying, "We're here to inspect these laboratories and these studies," it mobilized efforts and quickly a couple of countries got their own regulations and developed their own inspection programs that were compatible with FDA, and FDA entered into a memorandum of understanding (MOU), where it's almost like a treaty. We accept their word. They inspect the lab; they give us a report that they just tell us that that lab is in compliance.

JS: You refer to the revision of these regulations as wonderful. Why? What was the improvement in the revision of these regulations?

JH: The evolution of these regulations, not the revision. Because I think what they have done is to improve the quality of clinical research. They've improved the protection of human subjects in research. They've improved the method of documentation of the results of these trials, be that human trials or animal trials, such that the data that come to FDA, the reports that come to FDA of clinical, pre-clinical or non-clinical trials, the animal trials, have a higher probability of being of value. It is still possible for somebody to set out to defeat them if they really want to. If somebody sets out to commit fraud, they can probably do it, and they can probably still pull the wool over FDA's eyes, maybe not as easily, but crooks can be smart too. But I think they really improved the reliability in these trials, because if you follow them from a procedural point of view, it's unlikely you're going to make blunders. And I think that the dispersion around the world has really increased the quality of clinical research all over the world.

That's not the first time that happened. The U.S., in 1962, took a major step forward when the Kefauver-Harris amendment said that efficacy is based upon substantial evidence in adequate and well-controlled clinical trials conducted by experts. That standard, adequate and well-controlled trials, was something that was new to the world. It took a while to establish it in the United States. What is a controlled trial?

People who wrote the legislation maybe thought they knew what a controlled trial was. I'll bet by the time the regulations were written that definition had moved a little bit, taken more shape. By the time FDA really started to review NDAs that definition started to evolve rapidly.

It was under continuous revision. The more FDA learned, the higher the threshold of what was good-controlled trial went. There has never been a change in that regulation. It says the same thing right now essentially as it always did. Well, wait a minute, I guess when the NDA rewrite came through, they articulated it a little bit better and then amplified the guidelines, but until those regulations came out, words in the law served, adequate and well-controlled trials, and FDA kept redefining them. That was one of the things I guess the industry always complained about, you know, the moving target. Some of that is true and some of it I guess is inevitable, because as you learn more and science improves, what you're willing to accept goes along with it. So the combination of the concept of the controlled trial with the bioresearch monitoring processes that went with it all those decades later, I think is responsible for improving clinical research around the world.

JS: You started to go into a topic here that I wanted to address later on, your experiences. I mean you mentioned one in particular at Ciba-Geigy doing work with University of California, San Francisco (UCSF) and ties with the IRB there, and that's something I want to follow up on in general. But let me go on. I'm very interested to hear some of your experiences working with the various commissioners and general counsels with at FDA. Let's start with the commissioners.

JH: The first commissioner I worked for was Mac Schmidt's predecessor, Charlie Edwards. I only met Charlie Edwards once. I was in the Chicago regional office in 1971 when he came in. In 1968 I was in the Chicago regional office. In '71 I went to Winchester, Massachusetts as the

laboratory director for Radiological Health. At that time it was the Northeastern Radiological Health Laboratory (NERHL).

John Villforth asked me to come down once and brief Edwards and the policy board at that time on what we were doing up at NERHL. I remember that. The first time I had met Charlie Edwards, the first time I had ever met a commissioner, because until the Federal Reorganization Act, Radiological Health wasn't part of FDA. It was the first time I had ever been up in the commissioner's conference room in the Parklawn building. And I was at the end of the meeting. By this time Edwards was not terribly interested in what was going on. He was sitting at the table and he had one foot up on the table and playing with a pencil and rocking a little bit. I tried to run through what we were doing in that lab, changing it from an environmental radiation lab into an X-ray lab and what kinds of programs we were doing. He was very polite, and he asked one or two questions, but he wasn't terribly interested at all, and that was my only experience with Edwards as a commissioner directly.

I remember, one of the things that impressed me about him, he had a lot of hair, gray hair, not one hair out of place, didn't have his jacket on, his shirt looked like he was a Marine Corps drill instructor (DL) with no creases in his shirt, and he had a tie that I thought was just perfect for the combination. It's one of those images of somebody who pays a lot of attention to how he looks.

JS: You said that was the only direct contact you had with him. What sort of images of his tenure stand out as an employee of FDA, anything?

JH: No. I was too far away. It was the most delightful assignment I ever had. I was five hundred miles away from headquarters, and I was the director of my own little kingdom up there. It was a Public Health Service building, I was my own landlord. It was just terrific. We had our own maintenance crews, engineers, and everything, so it was a wonderful thing, and I didn't get down here every week like I did later on before I left the lab when we were looking at a transition. So I didn't have much of a perspective. In fact, I didn't even really know who his chief counsel was. Never had any interaction.

When I came down here in '74, I met Mac Schmidt and Sherwin Gardner, who was his deputy. Oh, I do remember that when Charlie Edwards was commissioner, Sherwin Gardner was in the job that Jake Barkdoll is in right now; he was the associate commissioner for planning and evaluation or something like that. He wasn't even a deputy. Who was that in those days? But when I came down here with Schmidt and Gardner, Peter Hutt was the chief counsel. The first thing I remember about Schmidt was when I got assigned to the Searle task force. I liked Schmidt. I thought he was a nice man. I thought he was on the shy side. Good speaker. Funny, I thought. Interpersonally he was a little reserved, but boy, you give him a microphone and he could be funny and he could be a good public spokesperson. I remember that even before I really had a chance to talk with him directly, he got crucified on April 16, 1974, when he went up prepared to deliver a drug lag testimony and got hit with all this conscientious objector stuff.

We covered that in the earlier talk. I think that that cast a very unfortunate shadow over his whole administration, because he was trying to dig out from under those hearings, the Dorsen Panel Report, and the commissioner's reply to the Dorsen Panel Report, which I thought Bill Vodra did a nice job on it, but I think it went into so much detail and was so long and so involved that it made, in retrospect, made it tougher on Schmidt than easier. If he had just kind

of accepted the report and said, “Yes, okay, we’ll tend to it,” and tried to walk by it, that report, like all of the others before it and all of the others since, passed in history more quickly. And you look at... Peter Hutt is the guy you talk to about this; because I told you that he wrote those two articles in the April 1983 issue of *Clinical Pharmacology and Experimental Therapeutics*. Of all of the studies, audits, and investigations of FDA drug approval process, the bottom line being there had been literally dozens, none has had really a lasting effect. All had a little effect and the organization changes slowly trying to accommodate, but all these grand, blue ribbon panels don’t leave much tangible behind it.

It is unfortunately the truth and it is fortunately the truth. It is unfortunate because a lot of people work very hard, they are honorable people, and they are committed people, and they genuinely try to do what is right. They try very hard to tell the truth as they see it so that the agency can be changed to accommodate what is either their version of the truth or the current version of social need for FDA’s regulatory system at that time.

The fortunate part about it is that FDA is stable enough so that it does not swing broadly on its anchor. The arc is rather limited. It doesn’t respond quickly to political pressure. It doesn’t change when vogue changes quickly. It stays along a fairly defined path. There is a lot of inertia in the system, because in general these wide swings of values don’t last long. They come back; they get to this end of the arc and it comes back. You don’t want an agency responsible for public policy, over 25 percent of all consumer expenditures in the United States, to vacillate. You want the thing to be reliable. Where is the standard? Well, the standard is FDA, and that standard moves within narrow bounds.

It’s a lot like our version of the British system. When the British change government, a few hundred people change jobs. The only person who changes his job in the department of the

Ministry of Health is the minister, who is an elected member of parliament. Everybody below him, including his principal deputy, is a career civil servant, and he keeps his job. In the United States when government changes, thousands of people change jobs. You've got the plum book that defines all of the appointed positions. The appointed positions are filled by people who come in with a mandate to implement the goals of the current administration's goals can be there at that pole and the administration that they're replacing could have been here at this pole, and what they're trying to do is drive the agency through the entire arch from one pole to another, from 3:00 to 9:00.

The stability within the agency, or its inertia, if you will, is that it doesn't go from 3:00 to 9:00; it goes from 5:00 to 7:00, and it takes a long time to get there. That's part of its strength and part of its weakness. It doesn't have flexibility; it's got stability. You can argue whether that's a societal good or a societal bad, but when you argue it, you have to take a historic perspective, not a snapshot. When FDA's at 5:00 there are times when it should be at 7:00. Most of the time everybody thinks it's just fine when the pendulum is down there between 5:45 and 6:15.

When I worked with Schmidt there was a sense that the pendulum was moving. All of my perspective now is in the drugs area, and I can't comment on what was happening in Foods, Veterinary Medicine, or anyplace else at this point – but everything was moving. We had the conscientious objector hearing which was saying we were treating our employees poorly. We had the bioresearch monitoring program that said we were not doing right in terms of monitoring the quality of clinical research, and that had to change. Dick Crout had been made bureau director just a couple of years before – I guess he was bureau director around '73 – and he had goals to improve the process scientifically.

I think Schmidt was trying to facilitate that movement in the right way. I mean we had really started the over-the-counter review (OTC). He was personally very interested in that. I just had a lot of respect for him; I thought he was a good guy. He was sat upon, unfortunately, by a lot of diversions caused by these conscientious objector hearings, and all of the investigations that went on for such a long time after that. They had the insides of FDA and drug area in kind of a constant turmoil, with Dorsen and then Frank Schwab who worked for Dorsen who was the investigator. He was the Joe Friday type. But I think FDA generally did well under his leadership.

Schmidt and Sherwin Gardner were good guy/bad guy, because Sherwin was the tough guy. Sherwin was the enforcer, and he was the guy who really ran the show. I had the feeling that they operated much in the way that Dick Crout and I operated his last year there after he had said he was planning to leave: a Chief Executive Officer/Chief Operating Officer (CEO/COO) way. Schmidt was responsible for policy; Gardner was responsible for operations.

Peter Hutt was the chief counsel then, and I have enormous regard for Peter. I think Peter is just a remarkable and brilliant guy, more opinionated than most lawyers, but smart enough to be able to really back them up. Very, very articulate. His goal was he was going to change all of the administrative regulations. Before he left FDA, FDA's internal processes, its administrative regulations were going to reflect his positions. I think he accomplished that goal before he left. Peter was a work of art. If you notice, there is only one office that I know of in that building that has its own air conditioner; it sticks out the front window, unless they've changed it. Hutt used to work nights and weekends, and nights and weekends in the summertime, there was no air conditioning turned on, so it gets to be terribly hot. Somehow Peter got an air conditioner put in the window. So his office is cool.

The first time I ever had a personal interaction with him, I hadn't been there very long and I was reading his early draft of a proposal on how we would run advisory committees. This was, again, the time of when freedom of information had just really passed and was ready to be implemented by the organization. The federal advisory committee acts were pretty new, and we were trying to adapt our policies to match those statutes. Peter wrote in one section that any federal employee would have access to a closed meeting. Any federal employee could attend a closed meeting of an advisory committee. I wrote him a note – it was the first time I had ever written him saying, “I think this is unwise, because this interpretation would let a DOB janitor attend an FDA advisory committee, and I don't think you mean this.” And I sent it off. Ten o'clock at night two days later the phone rings at home. Peter Hutt, he's in his office. He said, “I just read what you wrote. You're absolutely right and you're the only one who caught it. I'm going to change that and I really appreciate your looking at it from that perspective. Thanks.” I always remembered that.

Peter was also a very activist chief counsel. He worked very closely with Schmidt and with Gardner, and it at time almost appeared on the outside that Hutt was calling the shots, that he was the eminence grace, power behind the throne. I don't know how much of that is true, but I can tell you that the perception was strong enough that when Don Kennedy came into office and in his first talk to the Food and Drug Law Institute several months after he took office, he said that he wanted to thank his predecessor, Peter Hutt. And everybody gasped. Don realized what he had done and he afterwards went over and apologized to Schmidt.

Don Kennedy was the third commissioner I've worked for, and I remember meeting him shortly after he arrived. It was either that he came around to meet or we had a meeting with him. He looked like a professor with horn-rimmed glasses, tortoise shell, round glasses, naturally tight

curly hair, and I'll never forget this one either – he was wearing a green tweed or green wool suit with three buttons and he looked so collegiate, because he had these tattersall kind of checked shirts and a knit tie. I said, “This guy’s a college professor. He looks like a college professor. Yes, I can believe he’s a neurobiologist.” I was impressed with him right from the start. I liked what he said and the way he said it. He had about two-year tenure, and in those two years he underwent a metamorphosis. I mean I have never seen anybody get “Potomac fever” like he did.

Potomac fever. There’s a guy who quickly identified with the power and loved it and learned how to use it. We were really just digging out of all of the troubles we were having with Senator Kennedy over both drug lag and the conscientious objectors; we had gone through an intensely difficult period, because FDA was really just a whipping block. We were a handy tool.

See, I guess its part of my belief that Senator Kennedy really doesn’t care very much about FDA. He cared a lot about two things: embarrassing a post-Watergate Republican administration, and getting headlines, and FDA was a convenient vehicle to do that with. I think I told you last time that John Jennings once said that FDA was a slow-moving target that bleeds profusely when hit. That’s what was happening – FDA was getting hit. It got a lot of headlines and lot of television cameras. So during that period of post-Watergate – ’74 to the Carter administration, the Ford administration – FDA had no protections; we had the weakest secretary we have ever had. David Matthews, who was the president of the University of Alabama, and who knew from nothing about health, was no help at all, and as a result, not only did Mac Schmidt, but Dick Crout and anybody else that Senator Kennedy would get up on the stand, personally suffered.

Here we had a Democratic administration and a very, very appealing, young, dynamic, academic commissioner, who not only enjoyed testifying but was very good at it. He did almost

all of the testifying, whereas occasionally Dick Crout used to have to go up on the Hill to testify. Don Kennedy said, "Look, I know what you've been through. I'll do that. I won't put you in the position of having to get dumped by a Congressman, by Senator Kennedy or anybody else." As a result, through his tenure, I don't think Crout had to testify at all, or if he did very infrequently. Don Kennedy was terrific on the witness stand. He was bright, he was articulate, he was witty, and he was just smarter than all of them and did it in a nice way. And he liked that.

He became a very, very valuable asset of that administration. I think he would have enjoyed more power than he had. I think he would have enjoyed being secretary or something else. But it also became apparent that he was not in this job for a long haul. He had another agenda, which it turns out he did. I mean he was being groomed to become what he is: the president of Stanford University. We knew that he'd be going back to that.

To show you what the physical metamorphosis was like, the last presentation I saw him make, he was wearing designer steel-rimmed glasses. His hair had been, for some time by this time, professionally done. The hair wasn't in tight curls; it was very nice. He was wearing a very expensive blue suit and just the right color of blue shirt for television and just the right power of tie. You looked at this guy, and you said – if you held up a picture of him next to the neurobiologist who walked in, in '77-, are they the same people?" Don Kennedy also developed a little bit of a reputation of being a playboy. Sometime after he went back to Stanford and was provost for a while, then became president, he was divorced. For a while it looked like that might affect his tenure as president of Stanford. There were rumors that he used to play around. I saw him at a lot of the Christmas parties, including a couple that were off-site, and I saw him come, which I thought was unusual, kind of nice. But I liked him. I thought that he was just so goddamn great and fun to work with.

There was a couple of times when he testified that I would be in his backup team. He was getting questions from Congressman Sheuer about international harmonization – which is a great buzzword, everybody wants to do it – of regulatory requirements. They discussed why can't our regulations be the same as the U.K.'s so we could approve all of these drugs at the same time? I sent him a little note, slipped it to him: "Harmony not equal to unison." Kennedy didn't even make them believe that it was on the table. I don't think that anybody paid any attention whether he looked at it or not, but then without breaking his stride he said, "Well, Mr. Chairman, it is important to understand the concept of international harmonization, and to use a musical metaphor, singing in harmony, doesn't mean singing in unison." He just kept going on and he reached behind – I was sitting right behind him – and he just grabbed my knee and squeezed it. And I thought, "Gee, didn't miss a beat, just bang, bang, bang, right out."

Don Kennedy did something though. He really got FDA very actively going in international harmonization, and was personally responsible for two things. When the whole concept of working more formally with other drug regulatory agencies really became important, FDA and PAHO – Pan American Health Organizations, the World Health Organization's (WHO) regional office for the Americas – cosponsored a meeting on drug control in the American nations in 1979. When we had that meeting, it was the U.S., Canada, and about ten Latin American, Caribbean countries. It was right here at the Pan American Health Organization building in Washington.

Kennedy came and spoke, and I don't know if it was a plan or it just hit him and it was a good idea, but he said, "I think that this meeting is so successful that FDA is going to sponsor an international meeting of all drug-control agencies, cosponsored with the World Health Organization, in the United States next year." When that was all done, Dick and I looked at one

another and said, “Now what?” It was terrific, because what came out of that was we worked with John Dunne at WHO in Geneva, and we agreed that we would host a cosponsorship with the World Health Organization and the Food and Drug Administration, an international conference of drug regulatory authorities to be held in Annapolis, Maryland, U.S.A., in 1980.

We didn’t know who was going to come. We had gotten an agreement to use the Rickover Building, the conference room on the top floor on the campus of the Naval Academy. And lo and behold, we filled the room, just filled the room. It was set up with a rectangular table so everybody was facing in. But we must have had twenty countries, including China – not Taiwan, but China sent somebody. It just blew our minds. They had three people: one of whom spoke a little English and the other two couldn’t speak any English. Couldn’t figure it out. We had European groups that we had known because we had had independent meetings with them, some of them for years – the British, the Canadians. We had an interesting collection. We had the Saudis. We knew some of these people had drug regulatory programs – it was just amazing.

We put together an agenda for the meeting. It lasted a couple of days. We put together some social events, receptions, lunches, and we made ourselves forever unpopular with the press by saying, “No, we will not open the meetings to the press. These are going to be private working meetings.” We allowed the press to come for lunch to hear one of the luncheon speakers, lunch at the officer’s club. We had people spread around at several different hotels in Annapolis. It was really nice, and everybody I think got a lot out of it. And lo and behold, the concept clicked and those things are still going on about every two- to three-year intervals.

Dick Crout was the primary delegate; I was the secondary from the U.S. Two per country is what we were allowing. One or two countries had a third person, but they sat in the back; they weren’t at the table. I was the sole U.S. delegate to the second one in Rome in 1982.

I felt that there should have been two people, and I wanted Marion Finkel to come with me or Bob Temple or somebody, and I got shot down. So the U.S. was underrepresented in Rome, and I thought that the decision about that was FDA shooting itself in the foot. If Hank Meyer had wanted to appoint himself or Paul Parkman or anybody to go, even in place of me, fine. If they wanted me to go as a junior delegate, I would have gone. I felt that the U.S. should have had two representatives there, and we didn't. But we had a representative, FDA representative to FDA's programs. I thought we had a pretty decent meeting.

The biggest thing that came out of the Annapolis meeting was a list of people's names and addresses and phone numbers. Do not sell that accomplishment short, because until that meeting was over, we didn't know who our counterparts were in most of the countries. So what came out of that meeting was names, addresses, phone numbers, telex numbers, a few people even had telefax back then, but not very many – and an agreement that we would meet again. And a lot of talk about philosophy.

I was on the planning committee for the third meeting, which was in Stockholm in 1984, but I had left the agency by then, and Bob Temple represented the U.S. But I attended the planning committee meeting in Geneva at WHO headquarters in early 1983. At the plant, the planning committee was asked to make time available to listen to essentially pleadings from the International Federation of Pharmaceutical Manufacturers Associations (PMA) and the World Federation of Proprietary Medicinal Manufacturers, the World PMAs and the now World Non-Prescription Drug Manufacturers Associations, that they should be involved on the programs. I can remember very clearly saying, “No, I just don't think you guys ought to be there. I think that it's not good for you and it's not good for us regulators. There's lots of opportunity for the industry and regulatory organizations to interact. There's a lot of opportunity for the industry to

interact without the regulatory people there. The regulatory people need an opportunity to interact without the industry being there.” There was a lot of unhappiness about that.

When I joined Ciba-Geigy a number of years later and I became very active in the proprietary association, now the Non-Prescription Drug Manufacturers Association and I attended one of their meetings where they had some of the international guys there, because I was on the international committee. A guy walked in the room, looks at me, and said, “Can I come to this meeting?” I said, “This is your turf, not mine.” He said, “You’re a tough guy to deal with.” I said, “Well, I’m glad to meet you here, but I didn’t think you belonged in the International Conference of Drug Regulatory Authorities (ICDRA) and I still don’t, even now that I don’t, work for the agency anyway.”

The bottom line on that is, Don Kennedy was very facilitative at least and maybe seminally creative in terms of deciding that FDA was going to take a very active role in international organizations.

JS: Had this been done before on a formalized basis?

JH: Not worldwide. It had been done in the tripartite meetings for years, where the U.S., Canada, and the U.K. would meet. It would just rotate around, one country to another. And that still happens. FDA would meet occasionally bilateral with somebody from Italy would come over or from Germany. Mac Schmidt opened up Japan, and I guess I ought to give Mac the credit, because Mac went to Japan with the secretaries. FDA and the secretary of Health and Human Services (HHS), here, went and met with the minister of health and director general and pharmaceutical affairs general over there.

Then when they said, "Okay, we're going to put it at an operational level." In 1975 I was still working for Marion Finkel. Dick Crout was supposed to go. Dick didn't want to go. He asked Carl Leventhal. Carl was the deputy director of the bureau. Carl was going to go, and he had Ted Byers, who was the head of compliance, going with him. At the last minute Carl said, "I can't go." He said, "Have you been to Japan?" I said, "Yes." He said, "Will you go?" "You bet." I said, "Moreover, I've got a lot of interesting ties to the industry over there." He looks at me and said, "How?" I said, "One of my classmates from MIT is on the corporate staff of a drug company over there, and my uncle used to be the plant manager here in the United States for Dr. Jokichi Takamine, who started Takamine Laboratories here and he was the discoverer of epinephrine. He said, "Oh, you go." So that was terrific for me. Ted Byers and I went, and we had a number of days of meetings. The first time, there's a lot of bowing and looking at one another and not much accomplished; faces and names put together. You're here, we're talking. We didn't agree about anything; there wasn't any agenda to agree upon. There was an agenda to transmit information.

We had two interesting meetings that were outside of the straight meetings with the government people. We met once with the American Chamber of Commerce in Japan, their committee on pharmaceuticals, so we met with a lot of the Americans in Japan working for American drug companies at Japanese offices and lot of the Japanese people who had leadership positions for American joint ventures in Japan. Then the Tokyo PMA...hosted a reception in our honor at the Palace Hotel. Now, we were working very closely with a fellow in the American embassy in Tokyo at that point. He was an ex-Atomic Energy Commission engineer. We'd been doing a lot of international work. He had the position of the counselor for scientific affairs at the American embassy. Big fine job, one that I tried getting, but as soon as those jobs turned

over they just put career foreign service officers in them. They weren't out looking for people who had technical backgrounds anymore. There were two or three of those that came along, and I interviewed three times at the State Department, and they didn't fill them with anybody else, so I didn't feel badly that I had lost out to somebody, but what they had done was just change them over to career positions, and that was a disappointment.

But he was our liaison, and he provided somebody on his staff who was our interpreter. We went to the Palace Hotel and he made some remarks. First of all, you had the remarks made by the president of the Tokyo PMA – he spoke in Japanese and it was translated; he was bowing, yes, very nice – and then the guy from the embassy made some remarks and they were translated into Japanese. Then Ted Byers made some remarks, and then it was my turn. And I thought, everybody's standing here waiting to get at the food and the drinks and I've got to do something.

So I get up there and said, "I am really very, very pleased to be here, and I'm sure my uncle is pleased for me, too." And it got translated and everybody asked, "Did we hear him right?" I said, "Yes, my uncle. When I was a boy, my uncle was the plant manager in the United States for Dr. Jokichi Takamine." And everybody all of a sudden went, "woooooooh." The Japanese don't expire, they inspire, and they make a sucking-in noise. And I said, "when I was four years old I can remember going to Takamine's plant in the United States in Clifton, New Jersey, where they made Takadiastase" – and my olfactory lobes have memory banks that still remember what that smelled like." "I learned a lot from my uncle about at least one part of the Japanese industry. And I am delighted to be here, and I will extend my uncle's greetings to all of you." I got the best round of applause; it was terrific.

I had a number of people come over, and one of them turned out to be a really good connection. He was from Sankyo (Company), and he said, "Takamine Laboratories one of the

three companies that makes up Sankyo.” Takamine and two others were all merged, and Sankyo came out of the back after the war. He used to come to the United States periodically, and I met him here a couple of times; he came to FDA.

Then when I went back two years later, he came with me. We had another round of talks, a lot of the same faces, some in different jobs because they rotate. A fellow that I had met the first time as head of the safety division was then the head of a different division. He is now the counselor of the pharmaceutical affairs. He had been a director of every division; now he’s popped up. The counselor is like the deputy director, but he is more like the principal deputy who is responsible. He’s the real COO, because the director general works with the parliament and he had nothing to do with the day-to-day operations of the group.

This fellow’s name was Kumeo Shirota. I met him in Tokyo. Then I met him in Annapolis; I met him in Rome; and I’ve met him several times since. When I went for USP in June, we had dinner together. We’re more than just colleagues now; we’re getting to the point of being friends.

But on the second visit I took my wife with me. We had to do that right, because I was a government employee, and I had to fly on an American flag carrier, no matter how much more it cost. Very fortuitously, the day we were going and day we were leaving were the same dates that the Rutgers Alumni Association was having a tour go. So I got my wife onto that. Her airplane was next to mine. I was on a Pan Am flight; she was on a Japan Airlines flight. We left within an hour of one another. I went directly, non-stop New York/Tokyo. She went via Anchorage. I bought the land portion of her tour as my hotel and I met her at the hotel. So while I was in business meeting, she was out doing her thing, sightseeing and enjoying.

Ted Byers and I had said that in addition to the meetings that we wanted to have with our Japanese people, we wanted to see a Japanese pharmaceutical plant. And fortuitously, they set us up to go to Sankyo at the plant in the town called Hiratsuka, thirty miles south of Tokyo, because they wanted to show off their new small-volume parental facility. They picked us up in two cars. There were only two of us. They have their driver and then they have one of the high-level people sit in the back with one of us. It was this fellow who I had met the first time and who had since been to FDA once or twice. He got in the car with me and another fellow with Ted, and we drove down, and we had a chance to talk. I was asking him about the plant, and he said, "Well, basically, it's a very old plant, but this is a brand new facility." I said, "Still make Takadiastase?" "Yes, why?" I said, "Make it here?" "Yes." I said, "I want to see that." He said, "You what? Why do you want to see that?" I said, "Because I want to find out whether the memory of the fermentation smell is accurate." It's a peculiar sweet odor. Because there's really nothing to see; it's just a fermentation process. "Sure."

[BREAK]

We got down to the plant and met all the hierarchy, the plant manager and everybody. Then we had green tea, and afterward they took us through the SVP plant. That was really impressive. It was a good thing to see, because we found out that technologically these people really knew what they were doing, and that that plant was as good and as modern and as up-to-date as anything we had seen in the United States. As a matter of fact, on visits I had in June of 1989 when I went on this international meeting for USP, I saw some other companies in Japan and there's at least one plant over there that I don't know that we've got anything like it in the

United States. It's just incredible, almost totally computer automated. Enormous place that runs with almost no people.

We went through, and we had lunch. After lunch we came back and there was some question and answers, and then they said, "Do you still want to see the Takadiastase? I said, "Yes." Takadiastase is named for Takamine.

JS: Yes. Starch-splitting enzyme, right?

JH: Yes, that's exactly right. They got us in the car and they took us over to the other side of the property, old building, and get out and here's the plant foreman. You have very, very few people in a plant like that. There's not much to do except pour the stuff into the vat and pour it into the dryer. This fellow's almost standing at attentions. His eyes are wide open. Never in his life thought anybody from FDA was coming. I got out and I just went, (smells), bingo. That was 1978. I was forty-one years old, and it had been thirty-seven years since I smelled that smell, and it came back like that. My memory of that smell was absolutely accurate. We just walked through, nothing to see. You've got the vats and you've the drying, and you open it up, there it is. It's all lying out there. And I said, "I appreciate it. That's all I want."

The supervisor or the foreman or superintendent of that operation, whatever he was, he asked my host, "Why does he want to see this?" So my host told him about my uncle. As we were leaving, the guy comes over, bows very formally, and says to me in Japanese, which was later translated, "I want to thank you for your visit. It's a great honor. Please give my personal regards to your uncle. He must be very old now, and I want him to know that I am carrying on the tradition." I said I would do that. I said, "My uncle is, let's see, eighty." He's still around;

he's ninety-two now. But I said, "I will tell him." And I did, and my uncle was the happiest guy you could imagine. He really was.

That was really opening up bilateral talks with Japan, and it has continued. It's harder, much harder, than dealing with the Europeans, but vital.

Don Kennedy expanded relations to the world: meetings with Canada, meetings with the U.K. and some other bilateral meetings that had been happening, either ad hoc or the tripartite every year with the Canadians and the U.K. Schmidt opened the East; Kennedy the world. Through Kennedy's initiative, the U.N. has kept up the ICPR, but it has now become so big that, like most of the organs of the U.N., it's dominated by third-world interests and has lost its utility for the developed countries. Because the second one, in Rome, there were more countries than there were in the U.S. at the first one, which had more of the countries where there was some semblance of a drug regulatory program, and that was good. The one in Stockholm and the one in Tokyo after that were okay, but since then, they've gotten so big and so dominated by third-world interests, that even the WHO is losing interest. It's not keeping them going at two-year intervals; I think they're now on a three-year cycle, which is unfortunate. I think that if that doesn't change, they will die, because the world of drug regulations is not going to be dominated by third-world interests; it's really going to be dominated by groups like the European Economic Community (EEC), because it's very clear FDA is meeting with the EEC, and that's where the real action is, because that's like meeting with Europe. That's where the manufacturers are; that's where the major consumption is.

Kennedy's chief counsel was Rich Cooper, and I guess of all of the chief counsel's I have worked with, Rich Cooper is the one that I found the most interesting and one of the most far-reaching thinkers. I have asked Rich to speak at a number of meetings that I have been involved

in. I think when it comes down to nuts-and-bolts Food and Drug law, maybe that's where you want a Peter Hutt, for the history of Food and Drug law. Where you want something that's more abstract, I found Rich to be terrific in that area. He was also a Shakespearean authority; I found out that he used to read Shakespeare every night. He was one of those guys who start at one end and go through all of the Shakespeare plays and then start at the beginning.

I remember we got involved in an issue with non-tobacco cigarettes once. They were being labeled for "To break the smoking habit." The issue was, were these drugs? Is a habit a function of the body, because a drug is something that affects the structure, a function of the body? I forgot where we came out on that. I think that we finally decided they were not drugs. But it was interesting to listen to him try to formulate the policy, articulate the issues.

He and Don Kennedy were a good match, because Rich Cooper was a Rhodes Scholar. Incredibly bright guy, and he and Kennedy seemed to get along very well. These were two intellects that were well-matched. I think that they enjoyed working with one another. I remember one time at some discussion we were talking about alcohol, liquor. I can't remember the context, but I remember saying to Rick, "You know what Shakespeare said about that." He looks at me and says, "No." I said, "It's in Macbeth. 'Alcohol quicketh the desire that taketh away from the performance.' And it was a guard at the Macbeth castle who had been drunk and was commenting to Banquo or somebody that alcohol increases your sexual appetite, but when you're drunk you can't perform." Cooper looked at me and looked at me. "I've got to find that." The next day on my desk, there's a note. Macbeth, Act I, and then the exact quote. He said, "You were pretty close." (Laughter)

That was Cooper. Cooper was really a very good thinker, and somebody who I have kept in contact with since. I respect his mind and he's a wonderful, wonderful speaker.

JS: Would you say that the relationship between the commissioner and the general counsel, between Cooper and Don Kennedy in this case, was ideal? Relatively speaking?

JH: I don't know if it was ideal. I have a feeling that they communicated well. I think that it's hard to say what was ideal because ideal depends a lot on the style of the commissioner and the style of the chief counsel, and from what I could see, they communicated well. So it was certainly a good relationship from my perspective. I don't know it was ideal; I can't judge that.

Okay, Jere Goyan was the next commissioner. Goyan, I think, had a very unfortunate commissionership. It was very short, because he came in at the tail end of the Carter administration, and as soon as the election results were over, they literally kicked him out of his office. He was handled so shabbily, I thought that it was an embarrassment on the government. It was just terrible. When he came in, Pat Harris was the secretary of Health and Human Services, and I went down to the HHS building and listened to her welcome him and it was just so gushy and so wonderful. Here is a man who walks on water; everything's going to be great, just terrific. And that did not last long. Pat Harris, I think, developed an ego that was just insatiable, and she made life miserable, not only for Jere, but for Julius Richmond, who was the surgeon general at that time.

I think Goyan was also ill-served by his chief counsel, who was Nancy Buc. I found Nancy to be a poor chief counsel in my estimation. Legally she might have been okay, but the image that she portrayed was just not the right image. To follow somebody who was a Rhodes Scholar and a gentleman with someone who is absolutely crude... Nancy's language is vile. She used gutter language that would embarrass the men in the audience. She also had a direct

pipeline to Jody Bernstein, who had a direct pipeline to the secretary. I think that Goyan was boxed in between an overly aggressive, very pushy, domineering and crude chief counsel and a secretary who had her own agenda that inhibited communication with her first-line people. I don't really think she gave a damn about what was going on in their department.

Also, I think that Jere had a lot of tough issues at the time he came in. He inherited the cyclamate issue, as well as, the saccharin issue. Everybody has inherited these things. I mean they never go away. So he had his slice of them. He had the patient package insert issue, which was his, and there's where Jere shot himself in the foot. There were a number of things, and if you look at that paper that gave you today of my remarks at his twenty-fifth anniversary as dean of the College of Pharmacy at the University of California, I tried to review the major things that he was involved in. It would be more efficient to just look at that.

Where I think Jere went wrong was in an overly hostile attitude towards industry and to medicine. He started using the term "the overmedicated society, pill for all your ills." I just think he made the industry in medicine very unhappy because of that. They were caught too much in this mode of providing information that people need to protect themselves from physicians. I don't know that he intended it to be that way, but in retrospect, with ten years now looking back, I think that that's really the way they were perceived.

Jere's a very nice guy. He's a very gentle person. He caved in to this directive that he not communicate directly with me or with Dick Crout. He'd communicate with me, but she's not to communicate with, the head of the Bureau of Drugs; biggest bureau in the organization was important work. I think that was unfortunate. I think he should have just said, "I'm sorry. I don't agree with this, and I'm running the agency and I'm going to talk to whoever I like." I

think Nancy Buc didn't serve him well in this regard. I thought that Nancy should have made it clear that he should be the boss; she didn't do that.

Jere will always be my favorite commissioner for a very selfish and personal reason. When I got to be deputy director, I was acting for over a year. That was all through '78. I was confirmed in '79. I guess Don Kennedy was still there. After I was confirmed, I was put in for my promotion to assistant surgeon general, because it was very clear my predecessor had been an assistant surgeon general and was one that deserved it. It came through during Goyan's administration, because Goyan pushed it. He pushed it for three reasons: (1) It was the right thing to do because the job demanded it. It had been resisted because my predecessor was a physician, and just like civil service, the commissioned corps is much more willing to give high ranks to physicians than to non-physicians: (a) He pushed it because the job deserved it; (b) he pushed it because it was in his interest as a pharmacy educator to see a pharmacist get that rank; and (c), he and I liked one another personally, I still do. I still see him frequently, a couple times a year, and we are very, very good friends. I have served on the advisory board of the drug studies unit at the University of California for seven years or something like that. We got along very well.

There were some things I disagreed with, but never agreed with all of the commissioners either. I liked Jere a lot. I don't think Dick Crout did very much, because I think Dick reacted to him as most physicians did, that he was overstating the case about the overmedicated society, the physicians being insensitive. I think Goyan was right in a lot of respects: perceptions that physicians do a terrible job of informing patients about drugs and probably do tend to prescribe more than they should especially the older physicians.

My mother's going to be eighty, and she's on eleven drugs. Eleven drugs. You can't tell her that she shouldn't be on eleven drugs. Her physician's older than she is. But I think that he is a reflection of his generation and she of hers. She puts complete faith in him and when I jump up and down and say, "Why don't you go to somebody else?" She says, "After fifty years I'm not going to change." Even though he might be killing her.

When Reagan came in, the transition team just treated Goyan absolutely shamefully. They wanted him out of that office at once. He said, "I'm the commissioner until the day Reagan takes office." The day that he took office, they literally moved him out of the commissioner's suite and gave him a little office down the hall on some other floor until he could get his things together. The government didn't even pay to move him back to California. I just thought that was so shameful. You don't treat senior people like that. The fact that he's a different political party has nothing to do with it. Here was a man who came in, a distinguished educator, came in from a very prestigious university, in Reagan's own state, spent eighteen months, and then thrown out like he's baggage. That's what I'm saying about the advantages of the pendulum not swinging too much. There are too many people now who change jobs when the government changes jobs, and there's too many in FDA. At one time it was none, and then it was just the commissioner. Now it's down in the assistant commissioner levels.

JS: Who would be directly responsible for such treatment that the commissioner was receiving during the transition period? Would it be the Assistant Secretary for Health at that level?

JH: That was the transition team. These are all of the junior hotshots who come in yielding enormous power with damn little knowledge. It's one of the things in our government that I think is not something we should be very proud of. You can't treat high-level people that way and expect people to want to serve the government.

Okay, after Goyan was Art Hayes. Art Hayes and I have a very special relationship, because Art is the president of the USP and will be until March; then he becomes past-president. Art and I kind of hit it off right away. His wife's name is Barbara; my wife's name is Barbara. We have gotten together socially. I enjoyed working with Art. First of all, Art is a very surprising guy. He's a very slight man, physically, and yet he has this booming voice and he is a powerful orator. He is a truly professional speaker. Another bright guy, another Rhodes Scholar, he was at Oxford for a year, and a real Anglophile, and a great historian and good storyteller. And I guess I worked very closely with him on a number of things and always liked working with him.

I worked with him through some of the tough times. Dick Crout said he was going to resign the bureau director's job and work for another position in the Public Health Service before Art was appointed commissioner. So I met him for the first time when he was on the search committee for the director's job, because I asked to talk to the search committee.

I had no interest in being director, even though I had been deputy for a number of years. I had no interest in being a director. I said that that has to be a physician's job, but I wanted to talk to the search committee and tell them what kind of a physician they were looking for. It was interesting because on that search committee was, in addition to Art Hayes, Jim Deluisio. Deluisio is one of the trustees of USP. Also there was Wendell Hill, who was dean of the pharmacy school at Howard. There I met him for the first time. Then he became commissioner,

and still couldn't find a bureau director. His frustration was for the longest time trying to find a bureau director. There were a couple of candidates that they identified. One they were about ready to offer the job and there was some questionable financial thing his wife was involved in, so they didn't offer him the job. I think somebody else considered it and turned it down.

Dick really wanted to go because he had this opportunity at NIH and he had really backed out of day-to-day operations of the bureau. We'd agree that he was CEO, I was COO. He would take care of all the regulations that we were trying to get out on an NDA rewrite. He evolved policy stuff. Any day-to-day operations of the bureau were mine. For the most part, with little exception, that was it. So I used to go to policy boards. I used to represent that bureau at all of the external things that the bureau had to be represented at, because Dick really didn't want to do that. He wanted out. So I guess out of frustration Hayes finally merged Biologics and Drugs.

I saw right away that that was not going to work for me. I have several feelings about that. Number one, somebody coming in from the outside should never inherit a deputy. He should always have the ability to choose his own deputy. Hank Meyer had Paul Parkman as his deputy. And he had Cole Poms who is now dead, who is another right hand person, and the three of them were a very, very long-standing close-knit group, working together for years. And they came in with no great love for Drugs. Drugs and Biologics have always had a strained relationship. Any time they've had a relationship at all has not been a smooth one.

Hank was not a very consultative kind of a guy. It was a long, long time before he ever came over and talked to me at all. In fact, I finally said to Dick Crout, I said, "I know this isn't going to work. Here he's been named now for two weeks, certainly over a week, hasn't even called me." One of the times when Hank came over and talked to Dick, Dick said, "You've really got to talk to Halperin."

So Hank finally came in, opened up kind of a wall board, drew the organizational chart, and said, "You're here." What he had done was he'd taken two bureaus, called one the Office of Biologics. Out of the old Bureau of Drugs he tore out the six New Drug Evaluation divisions. That's it. "They're going to report directly to me, and the rest of this is going, that's going to be called the Office of New Drugs, and the rest of it is the Office of Drugs. You're going to run that." So I said, "Okay, so I'm not you're deputy." He said, "No, but I'm not going to have... Paul Parkman's going to be called the director of science, or director for science or scientific director, or something like that. Scientific director."

Well, over the next couple of months, you know, I started to feel I was part of the problem, not part of the solution, and I hated that.

I have principles about when it's time to leave. I live by three principles. Number one is, it's time to leave when you stop having fun, because if you're not having fun in what you do, don't do it. There are plenty of other things in the world that you can do. And money can't buy us bunk. The first thing about a job is it's got to be fun. The second thing is you leave a job when the intellectual balance is not tipped in your favor, in other words you feel you are contributing more than you are deriving. I always say you never want to feel that way. You always want to feel that you are deriving more out of a job than you are putting into it. You are learning more or gaining more than you're contributing, so that the flow of intellectual reward is in your favor. Otherwise, you get the feeling somebody's taking advantage of you. And the third principle is you want to leave when your departure is met with regret, not with relief.

I had a feeling I had tripped all three of these things: it certainly wasn't fun. I felt that I was still learning some things but I felt that the balance was rapidly shifting. And I had a feeling that Hank would really welcome my departure. When the Ciba opportunity came up and I

decided to accept it, I had a staff meeting one day when Hank was showing the next stage in the reorganization. He said, "Now we're going to do this and this and this," and he was talking about where people were going to be placed, and he said, "And Jerry's helped us out by quitting." By this time I was sitting back at the side of the room and I just shook my head and said, "Number three."

So, that was the one thing, you know, by this time Art had left. No, I'm sorry, Art had not left yet. He might have left and we might have been between Hayes and (inaudible) when... I can't remember whether the old witch was then or not. Either that or I left just before Hayes did. I can't remember when Hayes left, but I left May 31, 1983. I enjoyed working with Hayes. I thought he was really just a terrific guy.

Tom Scarlett was his chief counsel. I had known Tom for a long time, because Tom had been a staff lawyer working in the OTC program part of the time and then left and went out into private practice and then came back in as chief counsel when Hayes came in. So Tom was a comfortable guy to work with. Tom is very quiet, not a very outgoing guy. He's not the kind of guy who gets into a lot of small talk. I guess as a lawyer, he's a good lawyer. He's kind of a craftsman. He's not the guy who I always thought was the guy who got up and delivered the big pronouncements. He's not a Peter Hutt. He doesn't live for personal recognition and he's not the guy who's sought after all these years as the guru of Food and Drug law. Tom is much more work-a-day guy, and I think that if this tragic situation with Dingell had not occurred, Tom would be at the agency forever. I think he liked it, was comfortable with it, was good at it, and he would have stayed.

I got along very well with Tom. He had some very good people working with him in the general counsel's office and I thought that he was fine. I thought that he and Hayes had a decent

relationship. I don't know that it was ideal and I think that they're very different kinds of people, but I think that they worked together well.

JS: Unlike Don Kennedy and Cooper.

JH: Again, but that may be my perception. My perception was that they genuinely enjoyed one another. That may be a false perception. I have no idea whether they ever saw each other outside of the office. But they just seemed to be two very smart, aggressive guys who are incredibly bright. Neither one was going to be in for a long period of time.

JS: What sort of issues stand out in your mind that came up during the tenure of Hayes and how did he deal with them?

JH: Hayes came in for a lot of criticism for the authorities being rescinded back to the secretary. I think he did not fight hard enough and maybe actually thought it was a good idea when Schweiker required that anything that went into the *Federal Register* in the way of a major proposal or final regulation had his signature.

Now, I think, and I've told the National Drug Manufacturer's Association (NDMA) this a million times – that was a classic example of shooting yourself in the foot. The NDMA wrote to Secretary Schweiker. They wanted the OTC review to move faster. My first comment was, "Why? If anything, you guys aren't even cooperating very well with it. It's in your interest to drag it out as long as possible so all these old drugs still could stay on the market. Why do you want the thing to go faster?" Indeed, there's not unanimity in the OTC industry about that, but

that was the motivation. The board at the OPA went right to Schweiker and asked him to take a direct and personal interest in the OTC review.

Schweiker had a meeting. He had a meeting with the leadership of FDA, and I represented the Bureau of Drugs at that meeting, and the Proprietary Association (PA). We all sat at the table at his conference room at HEW in the Humphrey building. The PA said, “We think that this review would work much better if your office would take a personal interest in it.” I don’t know what Hayes could say about that. He was kind of new himself. He couldn’t say, “No, I don’t really think you ought to be involved Mr. Secretary.”

Well, a secretary doesn’t personally get involved – his staff gets involved. So that created work for people like Mary Frances Lowe, who had been one of his staff people on the Hill and came over with him to the secretary’s office. Well, at the assistant secretary’s level, they’re not going to let a document go from FDA to the secretary without being happy with it. So they started an entire bureaucracy of their own. Here you had FDA in the assistant secretary’s office to the secretary’s office. Then Office of Management and Budget (OMB) got involved because Reagan came in with deregulation, and remember the vice president had a specific task force on deregulation, therefore I think that one of the major problems that occurred during Hayes’s tenure was this multiple layer review between FDA, the assistant secretary, the secretary’s office, and OMB – anybody could say no, but they all had to say yes.

As a result, things were much, much slower than they ever had been before. And a lot of the major initiatives that FDA wanted to do more quickly suffered because of all the layers of bureaucracy and everybody writing something in. One couldn’t just pass it along or sign off on it; one had to play with it, send it back again, and somebody else plays with it.

It even got to the point where we sent up a whole bunch of proposed OTC monographs. These were actually the first of three publications. They were a collection of little ones. Included were vaginal products, douches, and aphrodisiacs. For aphrodisiacs, the recommendation was, nothing works. It's got to be a category two thing. But you have to review everything that was in the marketplace at that time and weigh why it doesn't work. The administration was just absolutely unwilling to put anything like that in the Federal Register. Not sexual kind of stuff. All the stuff got sent back, and it just sat around for a long time before finally somebody said, "Hey, look, we've got to publish this stuff. It's part of our obligation." Years later it got done.

Art repealed the proposed regulation on patient package inserts which made industry, medicine, and pharmacy happy, because this had been proposed before Goyan left. That was repealed and a moratorium was put on it. They were on also Art to impose a moratorium on directed consumer advertising. He got involved in a lot of other issues. A lot of the documents for the NDA rewrite came out as proposals during his tenure. So there were a lot of major regulations that were proposed during that period of time. There were a number of food issues he was involved in. Sodium was a big, big issue of his. Food labeling.

During his tenure, the Bureau of Drugs went through a number of major cutbacks. He eliminated the antibiotic certification program, which had been funded by industry. It wasn't costing the taxpayer a cent, but it really was unnecessary work, because the number of batches that failed certification was so few that it was not worth all of the testing. But that was a major problem with all of those people who were employed. What do you do with these people? Take them off funds that were supported through industry fees. A lot of them retired and a lot of them were absorbed. I don't think anybody was RIFFED (Reduction in Force). We discontinued the

poison control program. We reduced it way down in scope and blended in into another group. We discontinued the methadone monitoring program, and we cut back on a number of other programs.

One of the things the deputy used to do was make a budget presentation. As Dick Crout said, “The deputy proposes and the director disposes.” He’d spend it, but it was my job to propose it. I wanted to illustrate the fact that we got down to the point where we didn’t have any fat anymore. The next cut was bone and muscle. How do you do that? The Bureau of Drugs’ budget proposal was the most well-attended intra-FDA meeting ever, because people would come out of the woodwork. Nobody even knew who was around the board. They were literally sitting on the floor, perched in windows. So I knew I was going to have a large audience, and I wondered, how do I illustrate the point? It came to me.

We had an employee who was handicapped; he was deaf, but he could draw. He was an artist. So I asked him if we got him a large board and some colored pencils, if he could do a large poster for me. I walked up to the commissioner’s office, and I had the thing all covered up so nobody could see it. I had to put it up on an easel. I got up and made my opening remarks and blah, blah, blah. I tore this thing off and the place just broke out laughing.

It had a wagon train circle. Indians going around shooting flaming arrows at it. Between the circle of wagons and the Indians were some dead cowboys, laying down and they’ve got arrows sticking out of them and they’re labeled “antibiotic certification,” “poison control,” “methadone monitoring.” There were a couple of cowboys that have arrows in them and they’re crawling back to the wagons – they’re wounded. Those were the programs that we had to take cuts in and were proposing more cuts in. They were wounded. And within the circle of the wagons, here were those that we were protecting. Every one of the soldiers or the wagons was

labeled as to what the post marketing surveillance (PMS) program was, so you could see. Here were the resources. The wagon for the antibiotic certification program was burning. The one for the poison control program was burning, the methadone program was burning. The cowboys were dead. Here was some of the drug quality assurance out in the field. They guy had an arrow in him. We were going to have to reduce that, and a couple of other programs.

And I said, "I've always heard a picture's worth a thousand words. Here's our budget proposal, and if you want to see the numbers I can put the numbers up for you, but that's what it is." That was the shortest budget presentation I ever made and the one I got the most compliments about, because it clearly illustrated what I was talking about. People got it very quickly and saw the numbers; nobody argued about it.

JS: I do want to get you to Ciba-Geigy and find out a little bit about what it's like working at FDA from the other side.

JH: Why did I go to Ciba-Geigy? I guess this is a good place to start. What turned me on? There are two things. Number one, I had, by this time, decided that three criteria of when to leave had all been triggered. I decided then that day, because I went home that and I said, "Barbara, I'm going to leave. I don't know what I'm going to do, but I'm going to leave. I'm going to early retire. I just cannot stand this anymore. It was really affecting my health."

It really was. I was having cardiac arrhythmias. It was all stress-induced. Interestingly enough, there were four people in high level positions in the Bureau of Drugs who all had stress induced arrhythmias or PVCs. Everybody was okay (inaudible) there on those jobs. We were all off medicine; we were all okay. Hence, the time and pressure in those jobs I knew damn well

that it had been building up for some time that if I ever (a) was crazy enough, and (b) lucky or unlucky enough to get the bureau director's job, I would probably kill myself, because I just didn't handle that much stress that well. It probably would bring on a heart attack, so I didn't want the bureau director's job. I was delighted to have my deputy's job. I probably would have stayed if Dick Crout stayed or I could have worked with his replacement, but when the three criteria were triggered it was time to go.

My wife is a wonderful, supportive person. She said, "Look, you've got to be happy and I want you healthy. Whatever you want." I was in the office the next day and the phone rings. My secretary was away from her desk so I picked up the phone. The person on the other end...I said, "Jerry Halperin speaking." And she said, "My name is so-and-so. I'm a recruiter." I said, "Look, look, thank you very much, but..." She said, "Wait a goddamn minute. What? Are you so damn important that you don't have five minutes to let me describe a situation that may be a very important thing for your life?" I said, "Lady, you've got more brass than a pawn shop." I said, "Okay, you've got five minutes and I'm timing you." She said, "Fine. At the end of five minutes, if it doesn't sound like it's anything you're interested in, I'll hang up and thank you very much."

So she described the job, not a company – didn't say who it was – but a job. Now I had already thought the night before that if I left (a) I wouldn't mind trying industry. I always wanted to see whether the guys on the private sector side put their pants on the same way as the goys on the government side. And after, remember, I think I told you when I was at MIT in '73 and '74, I used to hear all this business about how industry is so much different and so much better and faster and crisper decision making and less bureaucratic than industry. I thought that would be fun to try. If I do that, I like OTC. Why? Because I'm a non-physician, and a

pharmacist can do more in an OTC company than he can in a Rx company, so I'd like to move to an OTC company. And I said, "I'd like to work for a start-up organization, because I don't want to go into another bureaucracy. I want to be a part of building something. I'd like to move to a smaller group. I'd like to be involved in management." Now how do I make all that happen?

Well, what she described is exactly that, and all I could think of was, "God is there somebody up there? It is Providence? What she is describing is exactly what I had said that I was looking for." So at the end of five minutes she said, "Time's up, what do you think." I said, "Well you hooked me." I said, "Yes, I'd like to listen a little more." So I said, "Well, don't tell me who the company is." She said, "Okay, I'll send you a ticket." I said, "Nope, can't do that either." She said, "I'll fly down and talk to you." I said, "Fine. Don't come to the office" "What?" I said, "I'll meet you in the cocktail lounge at the Holiday Inn on Wisconsin Avenue. She said, "What is this, secret spy stuff?" I said, "You bet. You're talking to me about a job with a drug company and I regulate it. You bet it's spy stuff. I don't want to know who the company is. All I want to know is more about the job, so I don't bias myself in my dealings with that company."

So she flew down and we met and again she described the company. In just the context of how it's organized, what the job is, it's multi-national, it's in New Jersey, so immediately I knew it was Roche, Ciba-Geigy or Heochst or Pharmacia. I started...it could have been any one of four or five. That didn't bother me too much, but the job itself sounded really very attractive. We didn't talk money or anything like that. She said, "Okay, what do we do now? I'll give you a plane ticket and you can fly up for an interview." I said, "I have to know how to do this legally. I'll call you." She said, "What will I tell the company?" I said, "Tell them we're talking and I'll call you back."

I went to Tom Scarlett and said, “Tom, how do I deal with this? I’m going to put in my retirement papers. I have an opportunity to talk to a company about a job. Don’t know who the company is yet. At my request they didn’t reveal it. But the job sounds interesting. How do I do it?” He kind of laughed. He said, “There is a way.” He called Jess Stribling in, because Jess used to deal with this issue for the lawyers all the time, because the lawyers were always going out for jobs, and they told me how to do it. And I called her back, and I said, “Okay, I will drive up. You can tell me the company.” She told me it was Ciba-Geigy, and I said, “Okay, that’s not a big surprise.” Told me the office was in Edison (New Jersey), not in Summit (New Jersey); that was a big surprise. New division, all that stuff I had known about. I said, “I will drive up or I will fly up myself. I don’t want any money from the company, because if I say no, I don’t want any record that I ever accepted anything from this company.”

So she set up appointments and I paid my own way and went up and talked to the people and was impressed with the people. The president, as I was leaving said, “Look, we’re ready to go to the next step. What do you want to do?” I said, “I’ve got to figure out how to do this. I know that this is peculiar, but it’s peculiar for me, too.” I said, “I’m a commissioned corps officer, regular corps, I can’t just give two weeks notice and get out. It’s going to take three months.” “Three months!” “I’ll start the process tomorrow. Three months only because I’m an ASG.” I said, “If I wasn’t I’d have to wait for the next retirement board, and we just had one, so it would be about ten months.” So he said, “Okay.”

I went back and I put my retirement papers in and talked to Tom and Jess again and they told me what the next step had to be. This time I had to disqualify myself from anything that had to do with Ciba-Geigy and put something in the file officially and get the papers moving, and I couldn’t deal with anything that had to do with Ciba-Geigy. The only other person I told other

than Hank Meyer – Hank Meyer, Gerry Meyer, Voyce Whitley, Jess Stribling, Tom Scarlett and Peter Rheinstein were the only people that knew. Peter was my deputy. I said, “You’re going to have to deal with anything that involves Ciba-Geigy and we’re going to have to do this in a way where it doesn’t tip off everybody else.

It became clear that I was going to retire, because the word got out that I had put my papers in. The word was also out that I was going to go industry, but nobody knew who it was. We kept the secret for a long time. Finally, about a month before my actual retirement date which had been established, it became known that it was Ciba-Geigy.

When I left I had a magnificent retirement party. I couldn’t believe the number of people there. Peter Rheinstein told me that it was the largest, most well-attended retirement party that anybody could remember – everybody but commissioners up to that date, which I was just astounded at. It’s rather humbling. I had a number of friends who had that huge room filled, and it was great. Art Hayes spoke and Gerry Meyer spoke, John Villforth, lots of people. It was a terrific send-off; I loved it.

When I joined Ciba-Geigy, I was maybe the twelfth person in this new division. Maybe in terms of professionals there was, maybe, I was the eighth or ninth. The rest were secretaries, clericals of some sort. I was the first guy with any kind of technical background. My title was vice president for technology. I was to run the Research and Development (R&D), the medical, and the regulatory programs. When I looked around there was nobody. The first day a grand manager came over and gave me a mark-up of a package of Acutrim, which is Ciba’s weight control product. This is the PPA product, phenylpropanolamine. He showed me the...package and he asked me look at the back corner. He said, “Is this okay?” I said, “What do you mean?” “Well is it okay? Is it legal?” I said, “Beats the hell out of me.” He said, “What do you mean?”

You're from FDA aren't you?" "Yes." He said, "Well, is this legal or not?" "I don't know." He said, "What did you do there?" I said, "Oh, okay, I supervised the guy who supervised another fellow who supervised another fellow who supervised somebody who would know whether this was legal. I'll tell you what; I'll figure it out though. I know where the regulations are and I'll figure it out and let you know." I found myself good at getting into the GMP and the labeling regulations in a way I never had before. I know from nothing about this. What he's asking me is to be a regulatory affairs officer in a company. I don't know anything about that side of the business. I started to learn.

Ciba was terrific. It was a good company, and I had an opportunity to build my own organization. When I joined them we had no products in the marketplace. When I left we were \$100 million a year. When I got there I was the twelfth employee. When I left we had about 160. When I got there we had one small chunk of one floor of a rented office building. By the time I left we had one and a half floors. So we were really growing organization. In my own organization, I was the first one in it, and when I left I had thirty-four people. I had a product development department, a medical department, a regulatory affairs and quality assurance combined department, which has since split. I was a member of the management committee. I wore two hats: I was the head of the technology department, but I was also a member of the management committee. I got involved in everything: business decisions, direct say in what was going on with the business. I learned so much; it was just wonderful.

I worked with some of the incredibly smart people, had a lot of very good friends who are still with the company. In fact, there weren't very many that left. The president left after about two or three years. He was a whiz at building new companies; wasn't as good at managing them. He went out to start another company; he's running that one now. The fellow who had been vice

president for marketing became president. He and I are good friends. It was a great group. Nine people on the management committee; seven of us used to go jogging together. We had a remarkably close relationship together. Very, very good group of people.

When I got to Ciba-Geigy I found that their major product was going to be phenylpropanolamine in the weight control product, and here I had just left FDA having signed off on the weight control proposed monograph that put phenylpropanolamine in category one as generally recognized as safe and effective, but with a big concern in the preamble about the potential effects on blood pressure. That's what everybody was getting worried about. A lot of rumbling within the agency, because we really didn't think it works. I said to the president, "Look, if you want me to take this job, the one thing I'm asking you for is enough resources to find out the truth about this drug. If it's safe and effective I'll get that for you, and we'll get this resolved at FDA. If it's not, I'm going to come to you and tell you that and ask that you withdraw it from the market. If the business decision isn't that way, you don't want to do that, and then I'll have to decide whether I want to stay or whether I'm going to resign. I'm a man of principle. Those are the ground rules." He said, "Okay."

He pretty well kept his word on giving me enough resources to study it. I could have probably done it faster with more money, but money was tight. Nevertheless, we did do some very, very good studies. One of them that I started is finishing up this year. Would you believe that NIH is studying that product? A consultant of mine and I were independently reading the *New England Journal of Medicine*. The lead article, by this Ph.D. physiologist, who works at the NIH metabolic lab in Phoenix, was about drugs that increase the metabolism of fat and how they measured that in this very sophisticated chamber. He called me, and said, "Did you read that?" I

said, “Yes, I just did.” He said, “Gee, that’s what we need for Acutrim.” I said, “I was thinking the exact same thing for PPA.” He said, “Yes, PPA, but certainly Acutrim.”

This was only two years ago, and we had already done a rising dose titration, looking at blood pressure effects with increased doses of phenylpropanolamine. We had already done another clinical trial at Rochester with a very good researcher where we showed conclusively a well-controlled trial that it does cause weight-loss over a placebo. It was a twelve-week double-blind placebo-controlled trial with 106 women. And I said, “Boy, the icing on the cake would be if we could find out that yes, not only does it work, but here’s how it works, because nobody knows.” Everybody thinks it’s an appetite depressant. There’s not even a lot of good pharmacological data for that, much less clinical data.

We talked to this fellow in Phoenix, and he happened to be in New York at a meeting, so I invited him to come over. He came over and we sat and talked, and he was really interested in what we were trying to do. I said, “Yes, it would be interesting taking a marketed product for weight loss, an old drug, and then trying to figure the science. Let me go back and talk to my people.” To make a long story short, they agreed. Here the National Institute of Health metabolic laboratory is doing this double-blind placebo-controlled trial of Acutrim in the most sophisticated system you can imagine, including putting people in a steel chamber for twenty-four hours and measuring all of the air they expire. Either the air they breathe out or the gas that comes out the other way, it’s all collected through this environment, and it’s analyzed for what’s in it. It can tell how many calories you’re burning over time, and it’s compensated. There are radar detectors in there, so the amount of kinetic energy that you expend walking around or shaking around, it’s attracted from that so they can see the effect on the basal metabolic rate. It’s

an incredible system. Only two like it in the world and the same guy built them both: one in Switzerland and one down there.

I was able to start up the development department where we actually got into some really nice formulation work with some sophisticated technologies, dosage forms, and advanced drug delivery systems, and we did a lot of the pharmacokinetic work, because that's what we are doing out in California. I started the medical department where we were doing the kind of clinical trials that I just described to you. I started the regulatory affairs department where we started new NDAs, that kind of stuff. Before I left we had our own quality assurance group, where we were taking more and more authorities back that had been done for us by our parent.

One of the last things I did for Ciba-Geigy is I attended a Ciba-Geigy leadership program. I was already negotiating on this job, but the whole management team went, and I went. I learned a lot, got a lot out of it. I also found out a lot about myself. We went through psychological testing such as the Meyers-Briggs profile. I found out that I'm a very bright (?), which I didn't think I was. I'm better in the abstract than I thought I was. But I also now understand why I tend to create paradigms, pictures, the visualized concepts.

"To me, the concept of our division was the zipper, and what we were doing was disengaging it." As we got larger and took on more functions, we separated from our parent and we did it ourselves. These functions were separate, and the zipper had to go out here and down here, and these functions were still tied to them. Over the six years I was with them that zipper did this. It was interesting to be a part of that.

I learned a lot about marketing. I learned a lot about the business sides of things and sales and how things happen. I could have used more time there, and I was enjoying it, but when this opportunity came up, I had to do this. This is a calling, and I just think that the opportunity

here is just something I can't pass up. I was looking at this record of the first 150 years of the that the executive director's wearing is the chairman of the committee of revision, the secretaries of the convention, and the secretary of the board. This is the one that's longest standing. They go back to Lyman Spalding in 1820 and there are only nine people on this list. Nine people in 150 years.

Cook in 1926, when USP 10 came out, to 1950. There was Lyman Spalding in 1920; Charles (Thomas?) Tickell Hewson in 1831; Goerge B. Wood, that was USP's 2 and 3; Franklin Bache, USP 4; Joseph Carson, USP 5; Charles Rice, was 1882 to 1901 and then Joseph Remington the rest of that – (inaudible) actually it was (inaudible) – Joseph Remington and then Cook and then Lloyd Miller, 1955-1970 and now Bill Heller, 1970-1990, and he's 10. And I'm going to be the eleventh one. And I look back at this list and know that I'm following in this line, that's...really humbling. Just incredible. There were more secretaries of the convention than there were chairmen of the revision. The title of executive director was so new that it wasn't even in this book twenty years ago. I could have any of a number of titles. I will automatically have four titles: executive director of the staff, chairman of the committee of revision, secretary of the board of trustees, and secretary of the convention. The working title I'm going to use is executive director and secretary which covers most of that.

JS: I would like to find out where you see USP and FDA fitting in together under your leadership.

JH: Closer than they are right now. This is one of the things we talked about before. FDA and USP have never been particularly close, and I think that there are a number of reasons for

that. Number one goes to USP's uniqueness. We are a private, voluntary organization. We are not governmental. We are unique in the world. Only one governmental pharmacopeia in the world. So we are separate. We tend to be kind of a bridge between the public and private sectors because we have representation from both. We have fifteen people from FDA who are on the committee of revision or on our panels. We've got a lot of people from industry. We are not dominated by FDA; we are not dominated by industry. Every once in a while the industry thinks we're dominated by FDA and FDA always thinks we're dominated by industry. We're not.

The British call us a QUANGO: a Quasi Autonomous Non-Governmental Organization. The unique status. People ask, "How are you chartered?" Well, we're not. We're not chartered in any legislation. We're a voluntary organization. A lot of MDs got together and said, "Hey, we've got to straighten out the drug supply that we use," and it's grown from there. We are the oldest continuously published pharmacopeia in the world. It's a system that works. We're chartered as a business in the District of Columbia, but that's got nothing to do with it. That's just so we can get our tax-free status.

Even when I was in FDA, we never really understood USP that well. In fact, I never really understood anything near the way I do now until I actually started working here. I think that part of the relationship with FDA is that FDA is obligated to enforce our standards, but they have no direct authority to create them or to change them. One can't change a standard. They can change an analytical method if they find that it is not appropriate for its use, but only after advising us and giving us opportunity to change it. They can change a name of a drug if they don't like the name, but only after they have given us six months notice to do it, and then they can only do it by examining all of the drug names. So neither one of those things has ever

happened. We never want them to happen. I don't think that anybody understands USP across the street more than that.

JS: I think there was a time, and I don't know how long it lasted, when FDA – actually it might have the Bureau of Chemistry at the time – when FDA didn't set the standards, but they provided reference standards, and there was a movement to have FDA responsible for this. This was in the 1920s. I don't know if it was before FDA, before the bureau became the Food, Drug, Insecticide Agency (FDIA), and I don't know how long this lasted, but there were a number of people in this country involved in drug regulation who felt that providing reference standards should be the role of FDA. Obviously, that didn't last.

JH: Actually, it goes the other way; we even provide the antibiotic reference standards. What we're trying to do is get FDA to transfer the authority for the monographs, which it has been going on since we discontinued the antibiotic certification program. But I'm going to give a seminar to FDA on the twenty-first of March, and one of the things I'm going to do is tell the people in FDA about USP, because I really don't think they understand how it's put together, what its governance is, how it relates to the industry, and the fact that it is not an association. Nobody pays dues here. Nobody belongs here. We don't have a constituency that we represent. We represent everybody. The message that I want to try to give FDA is that we're on your side. We can be part of the solution.

That's very apparent, because one of the concerns I've got right now is Commissioner Frank Young and Carl Peck have been saying that there are twenty-four drugs in narrow therapeutic margin that they're concerned about USP standards on, and they've never come over

and shared these things with us. Officially, they've never said, "Can you explain how the standards got this way, and here's what we think we ought to look at to change it." I just talked to Carl Peck about this the other day. I said, "Don't tell the Epilepsy Foundation that problem with carbamazepine is too much moisture. Tell us." We found out from somebody who attended the meeting and called us up. The Epilepsy Foundation can't help you; we can. Carl and I are starting to talk.

Clearly one of the reasons I was hired was to facilitate relationships between the two institutions. I feel very close to FDA. If it hasn't come out in the six hours that we've been talking to one another, then I've failed, because Mac Schmidt was right: "Once an FDAer, always an FDAer." And I feel very close to the institution. I think that I would never in any of my positions do anything that would be detrimental to FDA. At the same time I could roll over and play dead when I think that the people across the street are not doing something that is right or they're being foolish, and try to get it straight. I started talking to a number of my friends and colleagues over there and meet them occasionally. Try to do it little by little. I'm trying to pick up some layers and make things better.

In 1971, the FDA, the USP, and the American Society of Health-System Pharmacists (ASHP) started the drug problem product reporting program. In 1972, FDA issued a contract that USP got and ran it successfully for sixteen years. After I left FDA, for some weird reason, it went downhill. The relationships between the organizations became so bad that USP decided not to even bid the last time the contract came up for renewal. After declining to bid the time before that and having Hank Meyer and Dan Michaels come over here personally and tell Bill, "Please bid. We'll fix up the problems," we bid and got the contract. Nothing got fixed up. The next

time we just didn't bid. So FDA started its own program, the FDA DQRS, Drug Quality Reporting Service.

The presence of two competing programs in the market is not in the public interest. They're not in FDA's interest; they're not in USP's interest; they're not in the interest of the reporting pharmacist. Joe Oddis wrote a letter to Frank Young and Bill Heller saying that. He characterized the reason for the differences as trivial intergovernmental interorganizational competitiveness. To some extent he's right. I have just sent a letter to Jim Benson today in responding to his letter to Joe Oddis of January 22 saying, you know, "I agree with you. One program is in the public interest. Let's work together to bring it together." We have a unique contribution that we can bring to the table, a long-standing relationship with pharmacy and medicine that no other contractor can. We still account for three times as many reports as their contractor does, and it just seems silly to have two.

I think that unless I am a complete failure, over the next five years the relationships will improve. I hope they improve a lot, but I certainly want to see at least increased communication and some improvement. I see a lot of opportunity for USP in a number of forms, even apart from FDA. The major pushes for the next few years I see as coming in three areas. One is in biotechnology-derived products and our ability to create public standards for biotechnology-derived products and create standards that can be technologically in tune with what the needs of the industry are.

Next, I see increased emphasis in the drug information side on the USP Drug Information (USP DI). This is very important, especially in the electronic expressions of the data base, because the thing is getting just so big it's getting cumbersome to use, and people want information fast. Third-party payers are starting to look at the USP DI as a source of medically

accepted but unlabeled uses of drugs. We have a great leg up over the American Medical Association's drug evaluation's book, because we have continuous revisions, a public notice and comment process, and a consensus development process. We try to assure that there is a freedom of conflict of interest. I think that that is something that others don't do as good a job on, and we could be bigger, faster, better, and more up-to-date, and people are going to look to that. Especially when it's in an on-line form.

The third area is an international organization. We have already taken the leadership there. We hosted a meeting here February 8 and 9 with the representatives of the European, British and Japanese pharmacopeias. In my mind, we represent the big four. While the British pharmacopeia's is part of the European pharmacopeia, it's influence outside of Europe, like Australia, New Zealand, Canada, and the other commonwealth countries is still very great. The Japanese pharmacopeia is the major pharmacopeia in Asia right now, and with the size of their industry and their exports, they have to be one of the big four. We agreed that we would try to work together to harmonize our pharmacopeial requirements, and we'll do it in two ways.

Two concepts: one is forward harmonization and biotechnology is the example there. Forward harmonization is the concept of preventing conflicts in standards before they occur. If we're going to have standards, let's try to mesh and make sure that our standards don't conflict before we even get them in the book. The other is retrospective harmonization, which is the concept of straightening out the mess that we've gotten where we have conflicting standards right now, and we're going to try that in the area of excipients, pharmaceutical excipients, because those things are truly multi-national. They go all over. They go more widely around the world than the drugs themselves do. In the dosage formulations, we've got to get these things

straightened out. We're going to work for that. I think that over the next couple of years, those are the areas that we're going to be focusing on.

A fourth area is going to be in the interactive video area for drug information for professionals and consumers. We have two major projects going on there. And hopefully, we're going to have products in the marketplace this year.

JS: You gave us a little bit of background on that when we first met. Well, I think that's a good note to end on, the future of USP. But you hope that within five years you can start seeing evidence of this program that you just described?

JH: I would be very disappointed if I didn't. My goal is to bring USP into the twenty-first century – literally and figuratively. I want to make USP a vital source of standards and information on pharmaceuticals within the United States. I want to increase its prestige and influence around the world. While we will no longer be the single largest drug market in the world, the USP today is still afforded legal recognition in about forty countries. I want that to continue. And those countries outside of Europe, I want USP to be the sought for as the leader.

[END OF INTERVIEW]

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