National Cancer Institute History Project
Interview with Vincent T. Oliverio
Conducted on July 14, 1998, by Gretchen Case

GC: I want to make sure it's picking up. So, if you would just say your name.

VO: I'm Vince Oliverio. Well, you talked to the right person when you talked to Dr. Loo. He hired me.

GC: Dr. Loo hired you? Okay. I am going to start the tape. This is Gretchen Case at History Associates, interviewing Dr. Vincent Oliverio. Today is July 14, 1998. It's about 10:00 a.m. We're in the History Associates Inc., offices. So, you said I talked to the right person when I talked to Dr. Loo?

VO: Actually he was sort of my first mentor at the National Cancer Institute. I had been at the University of Wisconsin as a project associate, doing postdoctoral work with Charles Heidelberger. I started in the area of cancer chemotherapy there because he was the discoverer of 5-fluorouracil and was also well established in the field of carcinogenesis.

So when I came to the NCI, I had worked with fluorinated compounds in graduate school and at the University of Wisconsin, and NCI was working with 5-fluorouracil and other drugs and they were interested in recruiting someone who had a chemical and biochemical background. During my interview trip, which was throughout the East, I had stopped in Washington and met Dr. Loo and he took me around the laboratory area

there which was in the Experimental Therapeutics Laboratory. Dr. David Rall was the Chief of the Experimental Therapeutics Lab and Dr. Loo was one of the senior investigators in that laboratory.

I was hired as a fledgling investigator in January of 1959 and Dr. Loo's lab was right next to mine. So, we developed a friendship, now for thirty-eight years. We collaborated on many things but most of all he gave me a start there. I spent about twenty years in the laboratory, and during that time I became a Section Chief, and then eventually, when Dave Rall was made the Associate Director for the Experimental Therapeutics Program, I became the Chief of the Laboratory of Chemical Pharmacology. After that, in 1971, he went to NIEHS and then I took his position and Dr. Richard Adamson was appointed the Chief of the Laboratory of Chemical Pharmacology.

Then there was a reorganization of the Institute after Nixon signed the National Cancer Act. They reorganized the programs a bit and the head of our Division of Cancer Treatment was Dr. Gordon Zubrod. Actually, Dr. Zubrod was the Scientific Director of the Institute when I came in 1959. And I would say that probably my happiest years were those years when I was in the lab.

GC: Yes?

VO: Yes. That was great, because you made so many little new discoveries every day. It was during a time when chemotherapy was being developed, mainly through the efforts of the Cancer Institute, as an accepted treatment modality. There were many pioneers during that time that I was privileged to work with: Drs. Emil (Tom) Frei, Emil J. Freireich, and, of course, Dr. Ti Li Loo.

And Dave Rall was very important because he really assembled a great team of pharmacologists while he was there. I was really surprised he left, but I think he probably felt that he had contributed as much as he could to the area of cancer chemotherapy and was looking for new horizons and went over to Environmental Health Sciences.

GC: Although he has moved back up here now.

VO: Yes, I know he's back in the area now, because he retired and I guess after his wife died he remarried. I had some very happy days there with Dr. Rall. But the other thing is, I had a great opportunity to train a lot of young clinicians who came as clinical associates. You know, at the time, the Institute had recruited clinical associates who needed to satisfy their draft obligations for two years, so they came in under the Public Health Service Act. They were able to come to the Institute. And the nice part of it was the Institute was able to pick the cream of the crop. So they had some *very* brilliant young men that came in.

They would spend time in the clinic and then they could choose where they wanted to go in the laboratory to gain research experience. And I had the privilege of having some of those young men in my laboratory.

GC: Do you remember anyone in particular?

VO: Oh, yes. There were quite a few. There was Dr. Edward Henderson, who headed the Leukemia Service for a few years at the NCI and Dr. Vincent DeVita, who eventually became the Division Director and Institute Director. Dr. Bruce Chabner was another one of my clinical associates, who also became the Director of the Division of Cancer Treatment. W. Archie Bleyer, who is at M. D. Anderson Cancer Center and the head of pediatrics, was also in my lab. Dr. Robert W. Sponzo, who went up to the Albany, New York, Cancer Center, was another clinical associate. There were a number of postdoctoral fellows I had who were very good. Particularly, Dr. I. David Goldman, who left to head the Cancer Center at Richmond, Virginia, and is now at the Albert Einstein Cancer Center in New York. There were a lot of good, bright, young men who just wanted to learn how to click the test tubes and learn what the techniques are for doing some laboratory research and combining it with their clinical skills. So, to me that was very satisfying. That was great.

GC: To be allowed to teach like that?

VO: Yes. Right. And, of course, I've maintained those friendships over the years.

GC: That's really amazing.

VO: Yes. And then when DeVita came and became the Division Director, when Gordon Zubrod left to go to the University of Miami, when Dr. DeVita became the Division Director and eventually the Institute Director, I became the first Associate Director of the Developmental Therapeutics Program which now is headed by Dr. Edward A. Sausville. There were about two or three Associate Directors that followed after I did my tenure.

I spent five years directing the preclinical drug development program and we tried an experiment at that time. We would submit maybe about twenty thousand compounds, to screen them for activity in the mouse L1210 leukemia and P388 leukemia models and then into a panel of human tumors that were implanted in nude mice. We carried on that experiment for five years to see if we could bring any more compounds forward to the stage where they could be clinically evaluated, in phase I, phase II, and phase III and phase IV clinical trials after IND filing. It became apparent after five years that the mouse panel screen was not any more productive than the way we used the random screening approach in prior years.

And after that, the Institute reorganized and changed the screening approach—I think it was 1980. We had had a very large contract program that I directed prior to this in preclinical drug development. So I had quite a bit of experience in contracting and contract review. We did our own review of contracts and it became a no-no, because there were potential conflicts in having the intramural program staff reviewing its own contracts. As a result of the reorganization, I moved over to the extramural division of the Institute and developed the plan for the review of all the Institute contract programs by extramural committees. We had to do this because there was the Inspector General's Report that was critical of our review of the contract review process and that wasn't too well received by the Institute.

GC: Really?

VO: Yes. And rightly so. There were conflicts there. So they separated all the contract review functions which were originally in the intramural divisions to the extramural division and they formed a new division at that time and named it the Division of Extramural Activities (DEA). I went there as the Associate Director and while NCI was recruiting for a Director who had experience, particularly in peer review of grants and, to a lesser degree, contracts. The first Director of that Division was Mrs. Barbara Bynum, who had many years of experience in the Division of Research Grants at NIH. I worked with Mrs. Bynum from 1981 until she retired in 1995. Dr. Marvin Kalt was my last

Division Director. Essentially during that time I just did about everything. In fact, I think I created my own job.

GC: Did you really?

VO: Yes.

GC: Because this was a new Division.

VO: It was a new Division and there was really nothing described for "what am I going to be doing." I gave you that little blurb there which tells you what I was doing for the last eighteen years. And essentially I was the Institute's, what they call, RFA officer. Every program announcement and request for applications—they call them RFAs—went through my office before they were published in the NIH Guide. So any new initiatives that were going to be put out on the street for inviting, particularly grant applications from various universities, and industry too, had to go through my office to make sure that those initiatives were accurately described, they were clear, and that there was fair and open competition. And, of course, there were regulations that were set forth by NIH and the Department, the HHS, which had to be followed. So, that was one of my jobs. I initially coordinated all of the Division's small business innovative research programs initiatives. You've heard of SBIR (Small Business Innovative Research)?

GC: No.

VO: Well, it's a program which urges small business to apply and compete for small grants in various areas that are described in a booklet that's put out by NIH and it is backed by the Small Business Administration. Funds are transferred to NIH— like a set-aside—it can only go to small businesses, and there are certain criteria that they have to meet as a small business. Well, that program has gotten very large since I left. There's all kinds of literature at NIH about that.

Another thing I did while I was there was to be involved in misconduct in research, which was becoming a bigger issue in the last ten years. I was the Assistant Misconduct Officer for the Institute. Dr. Kalt was the Misconduct Officer and I was the alternate, but in my position I did all the leg work for many ongoing investigations involving NCI-supported extramural investigators.

GC: Oh, really?

VO: Well, because he had the final approval authority and things like that. Throughout government grant and contract funding agencies like NIH and the National Science Foundation, misconduct was a big issue, because there were instances where investigators were falsifying and plagiarizing data for publication in the scientific literature. They

could be prosecuted and have to return the money that they were awarded by government agencies to do the research. So, that was one of my other little jobs.

I was also Program Director for what they called the Academic Enhancement Research Awards, which was a very small grant program for investigators who were in undergraduate schools or investigators who were teaching and had graduate students. There were certain criteria that qualified them for money for that program.

Let's see. I also dealt with policy issues that were set up by Central NIH to make sure that—with regard to grant review and contract review—to assure that we adhered to those policies, that our committees adhered to those policies. I'm trying to think of some of the other things.

Oh, yes. I also coordinated the development of the agenda and the preparation and collection of information for the annual program review at the National Cancer Advisory Board, which would be the meeting at which each of the Divisions makes a presentation before the Advisory Board, to essentially say, “This is what we had done last year and this is where we are going.”

GC: But it was fairly formal?

VO: Oh, yes. Yes, it was fairly formal. Let's see. The other thing is I also did a lot of work on revising guidelines for grant processing and preparation and publication. I worked with Central NIH on those things, and that was a constant report. I also coordinated the preparation and publication of the annual report each year for the DEA.

GC: That's a fairly big job!

VO: Yes. I was also responsible for preparing a notice electronically which could be accessed by other institutes and alerted them to different initiatives that NCI was about to publish. The other institutes would query us if they had some interest in it or would want to share in putting the announcement out on the street and contributing their resources to any of the universities and colleges that wanted to apply for a grant. And that's very important, because you didn't want a lot of redundancy by other institutes. For instance, there was a lot of overlap between NIEHS and NCI for certain initiatives. And we would have to resolve those issues. Sometimes we'd meet with the NIEHS people and the program directors from both institutes and try and resolve some of those problems. You know, there's competition, let's face it, between institutes. And there's also competition for the money and for the grantees. So program directors have a tendency to become very protective of their portfolios.

GC: You wanted to make sure that research wasn't being duplicated? Was that it?

VO: Yes. Well, there's going to be some duplication, but as far as the expenditure of resources, if you could work together when money was tight, this would help. Like I say, most of my last eighteen years was involved in extramural issues. I worked a lot with the extramural community, scientists at different institutions. My first twenty years were mostly within the Institute and that was a period of discovery and a lot of excitement because we were being directed by the "father of modern cancer chemotherapy," Dr. Gordon Zubrod. He's still alive today.

GC: I know. I've spoken to him.

VO: Have you? I just finished reading his book.

GC: Oh, isn't it nice?

VO: Yes, yes. And, of course, we knew Kay, his wife. It's mostly about his family. But it was a real pleasure because he has always been such a gentleman. He had great vision and if it wasn't for Dr. Zubrod, we might not be where we are today as far as cancer chemotherapy goes.

See, during my early days at NCI, drug companies were not very interested in getting involved in cancer chemotherapy, because it wasn't a money-making proposition. So,

the Institute, in those early years, put together a nucleus of researchers who eventually went out to other institutions and stimulated the interest of the drug industry into cancer drug development. It took a few good people back at the Institute to get it going. I'm sure you've heard of a lot of those individuals.

GC: You did some of the early work on methotrexate. Is that right?

VO: Yes, yes. I work on folic acid antagonists, probably my greatest contribution there was methodology—being able to distinguish between a lot of the analogs and metabolites and providing the tools for studying the elucidation of the mechanism of action of the antifols. I also did a lot of work with a number of other drugs, the nitrosoureas. And I think I stimulated the Institute's interest in another drug that wasn't well known but was being developed by Hoffmann-La Roche over in Europe, and I alerted the Institute to it. It was procarbazine. Through my initial efforts, Hoffmann-La Roche provided the Institute with the first amount of drug for evaluation by the Institute. And I did some of the early work on the metabolism of procarbazine, which my colleagues and I initially reported to be also carcinogenic. But it's a very important drug in combination with other drugs in treating Hodgkin’s disease. You've heard of MOPP?

GC: Yes.

VO: Yes, okay. Well, one of the P's is procarbazine, and that really made that combination work. *But*, later on in some of those Hodgkin's patients it turns out that they develop other tumors, like leukemia. Well, work in our Laboratory of Chemical Pharmacology found out that procarbazine was carcinogenic in rodents and primates. There were many alkylating-type agents that are, you know, carcinogenic. But, at least we identified that and I reported it initially in a conference in Lugano, Switzerland. So I felt I made a contribution there.

And there were a number of other drugs that we studied using different methodologies such as radioactive labeling. I had a pretty good chemical background. I did a lot of work with radioactivity. I was able to do my own labeling of the drug and then we'd study its disposition in small animals and then in primates and dogs. Dr. Loo, of course, and I collaborated on a lot of that. That really was a lot of fun. In those days, when the research was fun, we even had opportunities to do some marine research.

GC: Really?

VO: Yes, up in Maine and down in Bimini and in Sarasota. We were interested, for science's sake, whether anticancer agents in marine species were handled in any way similar to what you find in the mammal. So that was the fun part of the research. But I think with the passing of the good old days, you don't get too much of that any more. You know,

maybe once or twice a year we'd go for a week or so, and we'd set up a whole mess of experiments. They would have the sharks and the skates and the rays all ready for us and we'd spend time doing some fundamental research, for example, we were interested in research on the blood-brain barrier.

GC: I remember Dr. Rall talking about that.

VO: Yes. Oh, yes. And actually Dave Rall did a lot of nice work, along with Gordon Zubrod and some of Rall's postdoctoral fellows who worked with him. I did some work with methotrexate in sharks and skates and rays with Dr. Dan Zaharko. We did some pharmacokinetic modeling and so that was science for science's sake. We learned a lot about those drugs that way. Nowadays NIH investigators don't have that kind of latitude any more, especially where public funds are scarce. The public might not be too happy about that.

GC: Were you allowed to just design your own projects and design your own experiments?

VO: Oh, yes. But we usually passed it by the Division Director for approval. A lot of fundamental concepts came out of some of the research like that, you know. But when I look back, I would say in those days we were performing much like a pharmaceutical research firm but in cancer chemotherapy, you know.

GC: Because the big companies just weren't doing the cancer research?

VO: Right. There were very few that would get involved. Lederle and Hoffmann-La Roche were involved to some extent, because they had produced some of the early antifolates and other anti-metabolites that were used in treatment of leukemia. Hoffmann-La Roche was producing 5-fluorouracil, and then the vinca alkaloid, vincristine, was being developed by Eli Lilly. But, you see, the problem was that it took a *lot* of resources, first of all, to run a screening program, to do the toxicology and the pharmacology, the formulation, the production. It just took big bucks to develop antitumor agents. At that time they had other marketed drugs that were keeping the companies going profitably.

Now that's changed considerably. I think what you're seeing at the Institute is that drug development efforts there now are really being modulated more and more. NCI and NIH are establishing partnerships with many of the drug industries, hoping that they will assume more and more of the cost burden in getting drugs available for patients with cancer and other diseases.

GC: Well, I was just going to ask you what brought you into cancer research at the very beginning? Is your Ph.D. in oncology? Is that right?

VO: Yes, I got my Ph.D. at the Cancer Research Laboratory at the University of Florida. It was one of the few degree-granting cancer labs at that time. Then it later was incorporated into the University of Florida Medical School. What brought me into cancer research? Well, my mother had cancer. She was one of the early patients with 5-fluorouracil and, in fact, when I came to NCI she was being treated at Wisconsin. When I came to NCI, they admitted her as a research patient in the Clinical Center, and she was put on several experimental drugs at that time. Dr. Frei and Dr. Zubrod talked to people at Wisconsin, where she was being treated initially, and she was transferred down here. But my interest in cancer was really family-related. It started before I went to the University of Florida and it just evolved.

GC: Was that the first time you'd heard of the NCI or the NIH, when your mother had gotten ill? Or was it a place you were aware of?

VO: Oh, yes. I was aware that there was a National Cancer Institute, because I was keeping up with the literature. When I was at the University of Florida, I took courses in carcinogenesis, biochemistry of cancer, and, of course, there were a lot of lectures and literature about NIH-supported cancer researchers there and I was familiar with some of the early work that they were doing. Therefore, I knew that there was an effort going at NCI. I had actually gone for job interviews at Hoffmann-La Roche, Sloan-Kettering, and several places like that, and I was very impressed with what was going on at Bethesda.

And, of course, Dr. Loo was very enthusiastic, and I felt that this would be a good place to pursue research. Of course, at the time I had a growing family and thought it would be a good area to settle in.

GC: That's right. You have eleven children, don't you?

VO: Yes. And thirty-six grandchildren.

GC: Thirty-six grandchildren.

VO: Right. And I have my last daughter getting married this August. So we're getting ready for a wedding, the last one.

GC: Oh, my goodness.

VO: She's twenty-eight years old, and thirty-six is not the end of it, I'll tell you, I don't think.

GC: That is a huge family.

VO: Yes, my oldest boy has nine children. Well, for eleven it's not a lot, but, like I say, this is my third career now. In fact, right now I've got five grandchildren waiting for me to go back to the beach.

GC: Oh, really.

VO: They're down there with my wife.

GC: Oh.

VO: We just drove up, actually we drove up because of my daughter. There was a shower for my daughter, a wedding shower, on Sunday, so my wife came back. But then she went back down yesterday with one of our daughters and her five children.

GC: Okay. Well, thank you.

VO: That's fine. You know, we do it all the time. Last week we had four or five grandchildren down there. It's a full-time job!

GC: I guess so.

VO: It's unbelievable. And then for this wedding, everyone's going to be there. They're coming from California, Texas, Rhode Island.

GC: You don't need to invite any friends. You'll have a whole church full.

VO: So, yes, we originally were going to do some traveling in Europe, but we put it off for this year. Last year we spent six and one-half weeks driving out West. It was fantastic. The trip of a lifetime, that we always wanted to take.

GC: You just drove?

VO: Yes. We just drove, my wife and I.

GC: How nice.

VO: That was after my retirement. We had always wanted to do that. You know, we'd fly over and never really get to stay anywhere. And, of course, we have a lot of friends and relatives all over the place.

GC: So you had people to stop and see?

VO: Yes, We could stop and see people. It was a lot of fun. It was just great.

GC: Well, did families at the NCI, did you get to know other people's families?

VO: Oh, yes. It was very, very close. There was a lot more opportunity there when it was smaller, and in the laboratory setting you get to know people very well, and of course, we were all a lot younger. I'm going to be seventy in December.

GC: Really?

VO: Yes. Well, look at Ti Li, isn't he amazing?

GC: I don't have any idea how old he is.

VO: He's over eighty, and he's still active, we meet once a month and have lunch together.

GC: He's over eighty?

VO: Yes. In fact, he may be going on eighty-five. You wouldn't believe that, would you?

GC: No. I guess that's right.

VO: He still travels all over.

GC: I know. What was the campus like when you first came here, was it was much smaller?

VO: Much smaller. It was easier to get around. You got to know what other people were doing a lot easier than you do now. It was a very different time. It was during the years of Dr. Shannon, Jim Shannon, and it's interesting, because a lot of the people that he worked with up in New York eventually migrated down here to NIH.

GC: Because of him?

VO: Yes, because of him and this is a great place to work. One of my first technicians ended up marrying Dr. Richard H. Adamson here.

GC: Who was she?

VO: Charlene Denham. She was from North Carolina. She came from Women's College at North Carolina. I recruited her from there.

GC: Oh, in Greensboro?

VO: Yes.

GC: I'm from North Carolina.

VO: Oh, you are?

GC: Yes.

VO: Oh, okay. She was one of my first technicians. Then Dr. Adamson came as a postdoctoral fellow from Iowa and he worked in the next lab, and they eventually got married.

GC: Was that pretty common?

VO: Well, you know, there were many husband and wife teams at NIH in those days. The Weisburgers, John and Betty Weisburger I remember; the Tabors, Herb and Celia Tabor; Dick and Charlene Adamson; the Rabsons, of course, Alan Rabson and Ruth Kirschstein; the O'Garas, Roger and Margaret Kelly; the Whites, Julius and Florence White, just to name a few. There were a *lot* of husband and wife teams.

GC: Okay.

VO: They were all over the campus. Over the years policies evolved where some husbands and wives could no longer work side by side in the laboratory. It was okay if they were in another part of the organization. But I guess there were reasons for it that were beyond me. It was a very, very intimate environment. Everybody was interested in what the other guy was doing. We were a lot more sociable, I think, in those days. You know, when an organization gets big, that's bound to happen.

GC: Yes, it's just part of the lack of cohesiveness.

VO: Yes, right, right. I try to keep in touch with, you know, most of the people from those days. It's difficult, because some have passed away. That's inevitable, but it was just a lot of fun. Now I think there is more emphasis on, I think more politics have gotten into research here at NIH.

GC: Okay. Can you expand on that a little bit?

VO: Well, I think that we are expected to react to a lot of the pressures that Congress gets from the public. I think NIH was originally more like a university, where there was a little more latitude on how you conducted research. But since we are supported by American

tax dollars, this was inevitable as we grew. That's what I mean. Now we're building an Institute for every disease. I mean, there's an advocate out there, or advocates, for every disease. That's why I think during the Shannon years there was a lot of good basic research that went on that was not under those pressures. You know, drug development in a way started out from congressional pressure.

GC: Really?

VO: Oh, yes. Back then, 1955, they established what they called the CCNSC, the Cancer Chemotherapy National Service Center. That was the beginning, and that was a congressionally mandated effort, but it brought money to the Institute that provided funds for doing more research in chemotherapy. And then, of course, the viral oncology program, after the drug development, was also another one that had a lot of congressional pressure.

GC: Were you involved in that at all?

VO: No, I was never involved in the viral oncology program. But I think it was a good program, because a lot of the basic concepts evolved in the molecular biology of cancer from primarily a contract-supported program. There was a *lot* of good research, but a lot of money was spent in a contract program which had many critics. But it was cleaned up

over the years. I think it was a credit to the Institute. What more can I say? Overall, at least from my perspective, NIH was a great place to work. And for me, it was *real* good, because I got a view of it from several different aspects, from the intramural side and then from the extramural side.

GC: Was it hard to make that switch? From the lab to the extramural?

VO: Ahhh. Well. Yes, it was strange. I kept up pretty much on what was going on in drug development when I went to the extramural side. In fact, I worked for about three years with Dr. Hall, Tom Hall. He was a cancer chemotherapist and researcher from outside of the NCI. He used to be at Rochester University, then he was at Harvard University for a number of years, I believe.

We organized a symposium, which took several years, an international symposium, which re-evaluated older potential antitumor drugs that were discarded but not studied well. That was a lot of fun. We published that in a booklet. Dr. DeVita backed that one up. He was the Institute Director. So that was a lot of fun for me. For me, it was the transition project, you know, going from intramural to extramural.

I probably would have stayed completely in the laboratory but, because I did have a large family, I really had to take a position that was paying at that time a little better than

laboratory investigator earned. So that had a bearing on it. It's very difficult to get into an administrative position and get involved with policy issues and everything else, and then try to keep your laboratory going. Not too many people can do it. But I notice there are some Institute Directors that still do some research, and an NIH Director who does.

GC: Yes. He still has a lab, right?

VO: Yes. Right. He still has a lab and I guess he does a little bit, but he has fellows that work in there, so he can do it. It's a good thing, because I think it keeps him down with the real world, you know, of what's going on. But when you have a lot of responsibilities, you can't really do justice to what you're doing in the laboratory and do justice to directing or trying to get funds for other people's research and worry about the things that you need to worry about in running a large organization. I mean, you know, when you've got three or four hundred people you have to worry about, and some of them have problems, you just don't have the time.

GC: Did your hours change dramatically when you moved positions, like the time you spent at work or when you came in to work?

VO: When I was running the pre-clinical Drug Development program, it took a lot more hours and, to tell you the truth, I developed high blood pressure.

GC: Really?

VO: Oh, yes. And, in fact, that's when I had hypertension and I eventually had a heart attack right after I moved, but that's a number of years ago and I'm doing fine.

GC: Well, good.

VO: It was a high pressure job, even now, it's a very difficult job. There is a clinical network, that is depending on the Institute to provide them with drugs that they can put into the clinic. In addition, you have these cancer centers all around the country, you know, that need to be doing this work, and if they don't have the compounds to do it, they're going to close down their research efforts. So, the guys that are down there scraping up the compounds or looking around the world at exotic plants for new drugs and that, they've got to produce.

GC: That is pressure.

VO: Yes. I think I remember Dr. DeVita saying that after five years you should jump around to a new job every five years.

GC: Take a different job?

VO: Yes. Take a different job, he was an advocate of that. He thought that was good. I was going to ask him, why did you stay so long?

GC: He stayed longer than five years.

VO: Yes, yes.

GC: That must have been interesting to work with him as a Director, when he had started as your clinical associate.

VO: Oh, yes. He is a *very* bright person. He went through some very hard times while he was at the Institute, but he did a very good job. He was well respected. It made me feel good to see that he did so well. He's up at Yale now and doing all right. But, yes, it is sort of funny. I see a lot of these guys are doing real well. I hated to see Dr. Chabner go. He was also a fine person. A very bright young man and he was very good with his

fellow researchers, a real gentleman. So, it was really a pleasure working with him. Would I do it over? Yes.

GC: So you worked under eight Directors, right?

VO: Yes.

GC: From Heller all the way up to Klausner.

VO: Right.

GC: Do you remember, did you work closely with any of them?

VO: The closest Director that I worked with was actually Dr. Vincent DeVita, because I knew him well. And Dr. Rod Heller, he was only there for a year or so when I came to NCI, I was just a young upstart. I didn't know him well.

GC: You didn't hang out with the Director?

VO: Right. Then Dr. Ken Endicott came in as NCI Director from an extramural program. He started out as director of the CCNCS program before he became the Institute Director.

Then I did know Dr. Carl Baker and, incidentally, I still meet with him occasionally. We have lunch together. I knew Dr. Frank Rauscher fairly well from the laboratory days, where he was in virus research. Dr. Arthur Upton came to NCI as Director from New York, from the outside, so I didn't know him. And he only was here for several years.

GC: Two or three years?

VO: Yes, two or three years.

GC: He was the only Director who really came from outside the NIH during your tenure.

VO: Right.

GC: Did that make a big change in the Institute?

VO: He changed some things, yes. I have a feeling that some of the changes he made as well as changes made as a result of the Cancer Act prompted Gordon Zubrod to leave as he had responsibility solely for cancer chemotherapy. He also had to take responsibility for other cancer treatment modalities such as surgery and radiation. So there was some reorganization. There was a reorganization when I came in about 1960, and then there was another one in 1965 when that whole group went to M.D. Anderson.

GC: Frei and Freireich.

VO: Yes, Frei and Freireich. With the passage of the Cancer Act, in 1971, there was another reorganization. In 1975 there was some reorganization when DeVita took over as Acting Director. He was the Director of the Division of Cancer Treatment. Then the other reorganization took place while I was in the extramural program. I don't know if you've heard of the Bishop-Calabresi Report?

GC: Yes.

VO: Okay. I worked with that committee.

GC: Okay. Can you tell me a little bit about that?

VO: Yes. That was great. I really had a great time. And it was *really* a pleasure. That was one of my highlights. Dr. Marvin Kalt, my Division Director, is the Executive Secretary for the National Cancer Advisory Board, and as such he was also designated the Executive Secretary for this group of distinguished extramural scientists and clinicians. Well, he asked me to assist him because I had been around the NCI for a long time and I knew most of these people.

So I essentially did all the leg work of organizing each of their meetings over a period of a year and a half or so, two years. I got to know them very well, Mike Bishop and, of course, I knew Paul Calabresi from way back, because he is a pharmacologist, a clinical pharmacologist, and in the cancer field, so I knew him well. And I knew John Minna, who was originally from the Institute. There were others that I had known because of being involved in drug development.

But they were a very insightful group. They took their charge very seriously to examine the intramural program at NCI. There were a number of times that they would want some clarification from the historical perspective of, you know, a program or how it originated, what went on, and I was asked to contribute to that. I also developed most of the procedures for providing them with information to evaluate the intramural laboratory programs. In other words, I had to go to each Division and ask for their site visit reports and annual reports of the laboratories, and also I had to contact NCI investigators who were to be interviewed by the group and set up the time schedule for those meetings by the Bishop-Calabresi Committee.

So, it was a very demanding job. Sometimes we worked from 8:00 in the morning to 12:00 at night. I mean it. They were very demanding, because they didn't have a lot of time for conducting their business. When they came in for a couple of days, it was straight work right through. That was it. But it was fun. Dr. Kalt and I had the

privilege of commenting and doing some editing on their report. We recorded everything, notes. Over a period of a year and a half we must have met seven times. But the Institutes pretty much followed all of their recommendations and implemented them.

GC: Really?

VO: Oh, yes.

GC: So it was very successful.

VO: Oh, yes. I think it was very successful. It's interesting, because one of the co-chairs of the Committee, Dr. Michael Bishop, became Chairman of the NCAB. He succeeded a young lady from Duke University, Dr. Barbara K. Rimer. She has left Duke University and is now working for the Institute.

GC: I wanted to just go back for a minute. You talked about the reorganization after the 1971 Act that Nixon passed, the Cancer Act. What was your position at that time and what was the mood like at the Institute?

VO: Oh, okay. I was head of the Experimental Therapeutics Program, as Associate Director there. What happened is that we were in the Chemotherapy program at the time, and then the Chemotherapy program was reorganized and renamed the Division of Cancer Treatment. And what it meant is that experimental therapeutics and the drug research and development under Dr. Schepartz…

GC: Saul Schepartz?

VO: Saul Schepartz. Have you interviewed Saul Schepartz?

GC: I haven't. I haven't talked to him yet. I would like to talk to him.

VO: He could give you a lot of history, because he was with the CCNSC off campus a couple of years before I came to NCI. He is retired, too. He lives in the area, but you may want to talk to him, because he could give you a lot of insight into the origins of that program. He later became, he was head of Drug Research and Development and I was head of Experimental Therapeutics, which was mostly pharmacology and toxicology. He was head of the portion of the program that did screening, procurement, formulation and, let's see, I think that's it: procurement, screening, and pharmaceutical formulation.

Well, what happened is, after the Division of Cancer Treatment (DCT) was organized, a few years later Dr. Zubrod left and Dr. DeVita became the DCT Director and we combined all of Dr. Schepartz's program with my program and we renamed it Developmental Therapeutics. I was appointed head of the Developmental Therapeutics Program and Dr. Schepartz became Deputy Director of the Division of Cancer Treatment.

GC: Which was a new division, right?

VO: Yes. That was under DeVita.

GC: Okay. Now, I've heard a lot of things when the Cancer Act passed that there was a lot of talk that cancer was going to be cured by 1976, by the nation's birthday. Did you ever hear that kind of talk?

VO: Oh, yes. And, in fact, if you look at the *NIH Record*, you will see some articles on the front pages, "Cure in Five Years," and things like that. In fact, I might even have some of those old issues. But if you do get a chance to look at the *NIH Record* back in those days, you'll see those things like that. They've been saying it for years. It doesn't surprise me.

GC: So what did you think about that?

VO: At that time I said, "Oh, gee, that sounds interesting." You know, I thought, "Well, maybe there is a chance." But the older I got and the longer I was here, I said, "Well, you could take it with a grain of salt." So, I didn't take too much stock in that. Yes, it was interesting.

GC: Did you ever meet Mary Lasker or Benno Schmidt or any of the big kind of lobbyists who were working on the National Cancer Act and with other organizations?

VO: Only to be introduced at the National Cancer Advisory Board, because I was there when Mary Lasker would come to visit. And, of course, Benno Schmidt was on the Board. He was head of the President's Cancer Panel, the first one. So, I met him just formally but never really to work with him at that time. It's too bad, I should have, I have the minutes from 1970 or 1971 of one of the National Cancer Advisory Board meetings and you will see Danny Thomas listed there. It's really interesting. I did meet him and all that.

GC: You did?

VO: Oh yes, yes. It was fun.

GC: What was he like?

VO: Oh, *very* nice.

GC: Yes?

VO: Yes. Very gracious. It was fun. And, of course, later on Abby's sister, you know, Abigail Van Buren, her sister was on the Board for a while, Ann Landers. I mean, there were all kinds of interesting characters on the Board.

GC: The celebrities.

VO: Right, actually they were all very nice, you know, once you get to talk to them. But that was mostly socializing, you know, at the meetings, out in the hall and that, like that. But I knew some of the Board members very well because they were also scientists and really we had a professional relationship and collaborated on things. It was great.

You know, when you mention that Bishop-Calabresi, that was really one of the highlights, because what was satisfying about it is that when that report came out, the Institute did something. It just made me feel good that it wasn't all for naught. They addressed a lot of the concerns that were expressed in that report. It wasn't easy to do,

because there was really a lot, the reorganization was big, so you have now a well-delineated intramural program and extramural program.

GC: And it wasn't until after this committee's recommendations that it was really split?

VO: That's right.

GC: What do you think about that? Do you think it works better that way, to have that area clearly delineated?

VO: Well, I wasn't there long enough to say it's working better. I think time is going to tell that. I mean, I think we're going to need a few more years before we can really say how well it works. There were some advantages of having it mixed, with the intramural scientists involved in some extramural things, but it worried the extramural community because they suspected that funds were being diverted to intramural efforts that should be going to extramural research projects. They wanted a better accounting.

GC: Of the money?

VO: Yes. That's the name of the game.

GC: Money?

VO: Yes. I mean, it's not to say that they were deliberately doing something wrong or anything. It's just that the extramural community—especially during the years there was not much coming their way to keep up their research efforts, and you can't blame them—they wanted to know, "Well, what's going on at the Institute. How are they faring?"

GC: Right. Have things changed a lot in terms of money and resources and that kind of thing since you came to the Institute in 1959?

VO: Well, now I think things are pretty good for the Institute. Congress is being a lot more generous and a lot more responsive, but I think there's going to be a price to pay: They want to see results.

GC: They want to see some cures.

VO: Yes, and, you know, there a lot of good things that are coming down the road now. I think they are going to be doing probably a lot more in prevention and detection than they have in the past. And, of course, now there's been a biological explosion, and there's so much going on in genetic research, which I think is really going to open up everything.

GC: One thing I wanted to ask you about is the contracts versus grants kind of, there always seems to have been kind of a controversy about which is better.

VO: Yes. Well, contracts were suited to targeted programs more than grants. The problem with contracts is that an investigator who has a contract has to fit the bill. In other words, there are certain things that are laid down in the contract that they have to follow. They're being told: This is what you're going to do and this is what we want. We want this, x number of grams of this stuff and you've got to do that. And the contractor can't take that money and do a little bit of freewheeling research. A grant gives you a lot more leeway in how you approach things and a contract doesn't. But for some organizations, that's all they want is a contract, you know. They know what they're going to get.

GC: So they both have their uses, the contracts and the grants.

VO: Yes, right, right. Interestingly, the Institute now has a lot less contracts than they have had in the past.

GC: Really?

VO: And that was reflected in review, because in the Division of Extramural Activities we used to have a separate contracts branch and several grant review branches. Well, over the last year and a half, two years, the contract branch had less and less work to do in terms of review of contract proposals, and they were incorporated into a grant review branch as a separate section of that branch. So, the workload has gone down, and I think that's a reflection of less contract work in the Institute.

GC: Interesting.

VO: Yes. It is also interesting that the extramural community is very sensitive to the research community about the use of contracts. So there's a lot of pressure there. But the Institute is, at least from what I read.

GC: They're doing okay.

VO: Yes. But I do know that there is less review work going on as far as contracts are concerned and, therefore, organizationally, you couldn't justify having a big branch for contracts alone. So, that's what you call streamlining down or so.

GC: Dr. Loo suggested that I ask you about, is Dr. Jack Davidson. Did you work with him?

VO: Oh, yes. Jack, he's not well, physically.

GC: Yes. I was hoping to interview him, but he is not able.

VO: No, he's not. Well, he was a great researcher. We published together and had a lot of fun. He was a physician who came out of Columbia University and he really taught me a lot, because he was so meticulous.

GC: Really?

VO: Yes.

GC: Did you come in at the same time?

VO: He came to NCI about a year or two before me. But he can't get around. We used to, you know, meet, but his back is bad, he has diabetes and had some cardiac problems. But, yes, Jack and I, we got along great.

GC: Did you work on radiobiology kinds of things together?

VO: Yes. He ended up becoming head of nuclear medicine at NIH for a few years and then he went to Duke University for about ten years, to head Nuclear Medicine. And then I hired him back to NCI to help me in my program.

GC: You brought him back?

VO: Yes, I brought him back, because I needed someone to help me with one of the programs we had. I had heard that he was moving back to the area, because he has family in the area here, you know. So he came back and he worked with me at the Blair Building, when I had the extramural portion of the Drug Development there. I moved all over. I was on the campus, in Silver Spring, and then back to campus, and then I ended up in Rockville at the Executive Plaza, which I liked. I liked the Executive Plaza because it was great. I could go to Giant [grocery store] at lunch time.

GC: That is nice. What building was your lab in?

VO: Building 37, I had a lab for twelve years in the Clinical Center, on Six North, and then I had a laboratory on the fifth floor of Building 37.

GC: So, did you see patients, or were you only in the lab?

VO: No. I was mainly in the lab. The only time I saw patients is when we were doing a drug metabolism study and I went to get samples and things like that. But when I was in the Clinical Center, the only time I saw them was during a study that we were doing. Like the studies on methotrexate. We did the early studies on the physiological disposition of methotrexate in patients. Also dichloromethotrexate, and another drug called methyl-GAG.

GC: Methyl-GAG.

VO: Methyl-GAG. We did studies on methyl-GAG [Methylglyoxal-bis-guanylhydrazone].

GC: Dr. Loo talked about that.

VO: Yes. And we did studies on BCNU [1,3-bis(2-chloroethyl)-1-nitrosourea] and CCNU [1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea] in patients, also on one of the natural products.

GC: Dr. Oliverio, you were talking about the vinca alkaloids.

VO: Yes. And there were a few others. I did some early methodology work on some of those drugs that eventually got in to patients. Also we studied procarbazine

[N-Isopropyl-OC-(2-methylhyrazino)-p-toluamide·HCI] and, let me think, there were at least a half a dozen that I recall now where patients were involved.

GC: Did you work with Dr. Hertz and Dr. Li on that?

VO: No, no. That was done before I came.

GC: Right. I didn't know if you used any of his data.

VO: I knew Roy Hertz very well. He left NCI and went to George Washington University and the only time I saw him was down at the beach. Li is deceased. But I knew a lot of the early researchers that were at NIH and are, of course, no longer there.

GC: What was Dr. Shannon like?

VO: Well, I only knew Jim Shannon just from being introduced to him, but, you know, he was in Building 1, so I didn't get over there. Actually, he spent a lot of time down at the Hill, but my best relationships were probably with Zubrod, Rall, and DeVita, because of having worked with them.

I did a lot of traveling with Dr. Zubrod and Dr. Rall to various meetings. We had these periodic meetings at Southern Research Institute in Birmingham, Alabama, and in Rochester, New York. They all had to do with assessing the progress of certain protocols that were being followed in the clinic and just the usual meetings that you had. One nice thing, of course, in the early days and when the organization was not too big, every Friday the clinicians and the laboratory workers would get together and discuss their research, which was really great.

GC: Every Friday?

VO: Yes. And we got a lot of work done then. It was amazing.

GC: Was this grand rounds, or was this something else?

VO: No, no. This just had to do with the drugs that we were studying. That's when the clinicians came in and the lab workers would be there, certain of the lab workers, and we would discuss some of the toxic effects that were seen in the clinic and why wasn't this predicted in certain animal models, things like that.

GC: What would you say the general atmosphere was like when you were in the lab? I've heard a lot of people talking about kind of—I don't want to put words in your mouth, but how did people work together?

VO: We worked together well. There was a lot of excitement.

GC: Like where people would share ideas?

VO: Yes.

GC: And resources?

VO: Yes, absolutely, absolutely, y es. We shared resources all the time. I had certain setups that were being used by people from other labs. For example, when we were doing isotope work, we had this oxygen combustion technique that we perfected that was being used by other laboratories. We had published on it, just in a little flyer put out by the New England Nuclear Medicine Corporation, and pretty soon we were getting inquiries from other labs around NIH. I worked with Dr. Jack Davidson and a bioengineer on developing this technique and it helped to facilitate drug disposition studies. The oxygen combustion flask technique. Davidson, Peterson, and Oliverio, and Dr. Dick Adamson's wife, Charlene.

GC: Part of the husband and wife team. What would you say your favorite thing was about working at the NCI? Either your favorite moment or your favorite kind of work or the thing you're proudest of?

VO: Probably some of my original work with the antifolates, I think that opened up the way for doing studies with the antifolates down the road, and first of all, it took a lot of hours and hard work and it paid off, because it's a technique that has been used for years now. So, that was sort of satisfying.

GC: And exciting?

VO: Yes, and I did like the work. When we did some patient studies it was sort of fun. We'd have to be there until midnight, you know. You can't turn it on and off. Or we'd have to work in the cold room. I'll never forget it.

GC: What was that like?

VO: They had these walk-in lockers where you had these columns set up which were used for separating different components in biological fluids and things like that. So, to prevent decomposition the experiments were performed close to zero degrees. You'd go in the cold room all bundled up.

Of course, we had some other studies going. We had lobsters in a tank that we were using for some of the studies. We had them flown in from Maine. We were doing some plasma protein-binding studies and we'd periodically withdraw their plasma, which was bluish-gray. When we were finished with the experiments, we would cook the lobsters and eat them.

GC: That's a nice little perk!

VO: Yes, those protein-binding studies were very interesting. Instead of throwing the lobster away, we ate them, steamed them and ate them.

GC: Did you live fairly close to the campus so it was pretty easy to get in?

VO: Yes, I only lived about fifteen or twenty minutes away. There were a lot of nighttime experiments; sometimes I was able to come home for dinner and had to go right back.

GC: Oh, really? Weekends too?

VO: Weekends too. Yes. When you set up some of these experiments, they run you.

GC: You don't run them.

VO: No.

GC: But then when you switched to the extramural work, you didn't have to do so many weekends?

VO: No, usually I didn't have to go in on the weekends with the extramural work. It would depend. Now, when I was working with the Bishop-Calabresi committee, or in meetings like the National Cancer Advisory Board, which could extend into the evening or next day, then all bets were off. You had to be available.

GC: Right, they ran you again, right?

VO: Right.

GC: Well, I'll wrap up soon, but have I left anything out that we haven't hit on? You've hit on a lot of my questions without me asking them.

VO: Yes, not that I can think of right off. My memory gets dulled sometimes.

GC: How much did you work with Frei and Freireich and that whole team of leukemia researchers? Did you work with them?

VO: Well, of course, Freireich ran the Leukemia Service and Dr. Frei the Solid Tumor Service. I usually worked with their fellows or clinical associates who were under them.

GC: Okay.

VO: However, as far as discussion of the laboratory or clinical study results with Frei and Freireich, that's where ours was a purely intellectual exchange.

GC: And this might have been like at the Friday meetings?

VO: That's right. When we went to meetings out of town, we had mutual discussions of our reports and things like that. I know them both well, and it was a pleasure to have worked with them.

GC: So then someone like Dr. DeVita would come in and work under you but also under Dr. Freireich on the clinical side?

VO: Right, right. On the clinical side. Actually, at the time that DeVita came, Dr. Paul Carbone was the head of the Solid Tumor Service, and DeVita worked under him in the Clinical Service, but in the lab he was under my tutelage until he left.

GC: Okay. So, did the associates do like a year in the clinical side and a year on the lab side, or did they mix it up?

VO: Well, usually the first year, most of the first year, was in the clinic.

GC: Okay.

VO: Then I had the associate for the second and sometimes the third year; usually they would apply for the third year. After Dr. DeVita finished his associateship, he went away to Yale to finish his residency, and when he came back, he came back as an investigator in the Solid Tumor Service and then my technician, Charlene Denham, went to work for him.

GC: Did every investigator have, like you just said *your* technician, did you have a certain person who was assigned to assist?

VO: Yes, someone who you could depend on to assist you. Sometimes you'd have a couple technicians, depending on the work load. When the clinical associate came in, you'd be surprised how the technicians could assist in training them.

GC: Really?

VO: Oh, yes, very important.

GC: In terms of the hands-on you mean?

VO: Yes, because the technician was always trained to do what the mentor could do. And when the mentor was not there, the clinical associate could turn to the technician and say, "Well, how do you do this?" And of course, in publications of our experiments, if a technician's input was highly significant to the results obtained, they would get co-authorship.

GC: The technicians would?

VO: Yes.

GC: Or the associates?

VO: The associates *and* the technicians.

GC: Oh, really?

VO: Oh, yes.

GC: Oh, good.

VO: Like, let me see. In the bibliography of publications see, Oliverio, Denham, Davidson, "Oxygen Flask Combustion in Determination of C^{14} and H^{3} in Biological Materials." Oliverio and Denham, "Synthesis of Methylglyoxal-bis-guanylhydrazone-C^{14}."

GC: Methylglyoxal?.

VO: Bisguanylhydrazone. See, Adamson, Oliverio, Denham, and Venditti. There she is again. John Venditti.

GC: Venditti's name has come up a few times.

VO: Yes, And Davidson, and Ed Henderson in the bibliography.

GC: It looks like a lot.

VO: Anyway. That's about it.

GC: Well, you covered all my questions. That's an awful lot.

VO: Well, if you have any more, just give me a call.

GC: Is there anything else you'd like to add for the record, the historical record?

VO: No, that's all right.

GC: Your moment in history?

VO: My moment in history.

GC: So, you're glad you were there.

VO: Oh, yes.

GC: You were there thirty-eight years?

VO: Thirty-eight years.

GC: That is a long time.

VO: Yes.

GC: Was it a good time though?

VO: Oh, yes.

GC: Do you miss it now that you're retired?

VO: A little. But I have so much to do now, it's just unbelievable. I mean, I'm busy all the time.

GC: Well, I know I had a hard time getting you even once. This is the first time I've done an interview without ever actually speaking to the person.

VO: Is that right?

GC: I never spoke to you. We traded phone messages!

VO: Yes, right.

GC: And I talked with your wife.

VO: Right, we have so many children, you know, we end up babysitting and doing all kinds of stuff. Traveling. So, that's another phase of my life. The one thing, and I always tell this, my number one priority was always my family. My number two priority was my work. I never got that mixed up.

GC: That's important.

VO: Yes, right. I've been married forty-five years this month.

GC: Congratulations.

VO: Thank you.

GC: That is a big anniversary. Congratulations.

VO: Right, and we've been very fortunate, we've had a good life. It wasn't easy.

GC: But it sounds like it's been very good.

VO: Right, right, yes, it is, and you see a lot of little guys running around.

GC: All thirty-six of them.

VO: Well, the oldest one is twenty-two, so.

GC: Your oldest grandchild is twenty-two?

VO: Yes. No great-grandchildren yet.

GC: Well, give them a few years.

End of interview