This is an interview of Dr. Robert Manaker, who was Deputy Director of the Viruses Cancer Program, taken on March 9, 1995. The interviewer is Dr. Carl G. Baker, former Director of the National Cancer Institute.

Baker: So, Bob, give us a little bit of your background first?

Manaker: Well, I got my Ph.D. in 1953, at Rutgers University, and I stayed there as a postdoc. We had gotten wrapped up in working on an actinomycin. I had an undergraduate student who had gotten a culture producing an actinomycin, and I had then purified the material, ran it up into a crystalline form, and it looked as though it was a rather unique and single compound.

Baker: Waksman was the head of it?

Manaker: Selman Waksman was the head of it, yes. And, of course, he was enthused about it, and the yields were very good and the crystals were very nice and clean. I separated them on salicylic acid columns and we called it actinomycin D. So, actinomycin D, I guess was first used by Sidney Farber with leukemic children. He came around to the labs once, and he wanted to treat a kid who had a renal tumor, I believe. He asked how much Waksman wanted for a gram, and Waksman promptly said $6,000 dollars, which was about what he was paying me, you know, for a year. So, he got his year out of me *gratis*.

Well, in any event, it got rather tiresome thinking in terms of doing this kind of work, but it came rather naturally, you know, because prior to the war I had worked for about 5 years at General Aniline and Agfa Film in their laboratories, as a chemist, in which I had to do all of the lab work. This kind of activity, that is the purification and so on, was rather familiar to me at that time, so it went rather easily.

What sort of broke this, let's say, "rut," in which I was finding myself, was an offer from Vincent Groupé to come into his virology laboratory at Rutgers and sort of help run the place, make life a little easier for him and, at the same time, he thought that he

should give me a little "plum," as he called it, and he said I might get involved in cell culture. Well, cell culture, at the time, was rather new and people were taking little bits of chicken embryo, hearts and things, and putting them into plasma clots.

Baker: Before that, did you consider yourself a chemist?

Manaker: Well, I didn't like chemistry for one particular reason; too many people ended up in Arizona because of lung problems and such who were in chemistry. And since I had worked for a really large concern, General Aniline, it was part of the I.G. Farben industry, and then also became united with Agfa Film, General Aniline and Agfa Film, I did a lot of dye stuff work and such, and the fumes and things that one was exposed to, not just in the lab, but in the plant in itself, was just a little bit too much, and I had a tendency to become bald too after a while, so all of these things indicated that I'd rather do something else. And when I did go to complete my university training it was to get into biology. I settled on microbiology. It was easy to get into Rutgers, I suppose, because I lived close to the university.

Baker: And Dick Rauscher was another student at the same time?

Manaker: He was another Rutgers grad. He was in Groupé's laboratory also. He was still and undergraduate while I was a graduate. I had taken my graduate work under a fellow named Robert Starkey, another old hand under Waksman.

Then Groupé, at that time, was interested in the usual influenza viruses, the PR8 virus and such stuff, and this is the reason we had a lot of chicken eggs around. I began my cell culture explorations with chicken material. But, you know, it's hard to realize how early it was then. It was about that time that Wilton Earle, down here at NCI, was attempting to make monolayers, and he was using perforated cellophane as an overlay and shoving cells under that and getting some kind of outgrowth. I think Wilton Earle and George Guy were the people right there who really contributed.

Baker: They were the pioneers.

Manaker: They gave it the start. And that was right about that early '50s time.

Baker: Ross Harrison would perhaps be the only other name that comes to mind as a pioneer, at least in the U.S.

Manaker: Right. And then, in fooling around this way, making a medium for cell culture was a little difficult, but it had to be rather simple because there wasn't much money at a university, and I made up my media with materials that I found up in the attic. There were a lot of amino acids and things, a little dust-covered up there, and I dragged them down. The surprising thing was that the medium I made apparently had a little magic about it because someone else told me that they had tried using the same medium ingredients obtained from other sources, and they didn't seem to work quite as well as mine did. And then they came in thinking that I had rocks in my head, but they took some of my own media from the freezer and, by George, it worked beautifully.

Baker: Did this have serum in it?

Manaker: Well, it had serum, but there apparently are small trace materials, and such stuff, particularly in older preparations, which often times make a great deal of difference in how things will behave.

So, getting back to making the media, the trouble I had with growing chicken cells was that there were a lot of round little fatty inclusions developing in the cells, and those cultures never really did very, very well over the long haul.

Baker: Now, was this before Eagle developed his media?

Manaker: Yes. This was about the time that he was developing his medium. I remember seeing his publications when they came out, and I thought, "Oh, joy, here's something simpler than the medium I was trying to compound, which I guess was a maintenance medium." Well, in any event, the thing in using these things and being a microbiologist, I read that someone had used some of these bacterial media to supplement their cell culture medium, and I happened on this tryptose phosphate broth, a suggestion to that as a

possible use in media, and I put that in, and it gave very, very pretty cell growth and the fatty inclusions weren't there and so on. And I had Rous virus, thanks to Ray Bryan. Ray Bryan had met Groupé and visited our lab on occasion. I think that here is where the real mention as a pioneer applies because it was Ray Bryan who essentially was supplying materials to people who were interested. He was an offshoot from Joe Beard's laboratory, I guess, at Tennessee there.

Baker: Duke.

Manaker: Duke. Yes.

Baker: But he was at Vanderbilt before that with Goodpasture, I think.

Manaker: That's right.

Baker: And then he worked with Joe Beard.

Manaker: Joe Beard afterward. And Joe Beard was working with the myeloblastosis virus, I guess. And then Ben Burmester up at the Department of Agriculture Regional Laboratory in East Lansing was working with lymphomatosis. Ray Bryan moved to work on Rous virus and brought it down to NCI and did some nice work quantitating this on a statistical basis.

When I got this into cell culture, I noticed that there were small areas of altered cells. They didn't roll over and die, they just rounded up rather nicely and grew out. And I began counting these, and they related very, very nicely to the dilution of virus I used and, not only that, but they conformed pretty well to some of the titers that Ray Bryan was determining on a chicken basis.

So, at that time there was an opportunity for me to come to NCI, and I thought I'd take advantage of it, and I did, and I had been working up this little assay procedure with the Rous virus, and Groupé and I thought we'd better get it on out, even as a little, short paper, before I left. So, I did. I submitted it to *Virology*. And apparently the Henles thought it was great, but a guy named Harry Rubin, out there in the West, who had an

undergraduate named Temin, didn't think it was that great, and he said he tried using it and somehow or other he wasn't getting the results I was.

Well, I suppose he got some of the materials that we used, that is eggs and things, and it worked beautifully and, as a result, he determined that apparently there was interference by leukosis viruses within his stock and that some of these viruses were defective, and he found that there was helper activity from the other virus and, as a result, they opened up this whole area which eventually led to determining a reverse transcriptase activity and essentially established the retrovirus group.

And this is why I felt that this whole area is worth a little bit of talk, because it was essentially the start into what grew up into important things for molecular biology with the transcriptase and such.

Ludwig Gross stopped into our lab in around those years--this is about the mid-'50s, somewhere around '54 or '55--

Baker: His first paper was '51, but nobody believed him.

Manaker: Well, that's just it. He was a lonely guy. I guess he was from the Bronx, and he had a technician, Yolanda, a very, very nice little lady, and he really seemed so helpless, and he didn't really know how to go about things, and was chatting with us on this. He didn't go in there and say, "Well, now let's get together and work on this," but he just chatted about what he was doing, looking for some suggestions and such, which we gave him. And it wasn't just that he was looking at a murine leukemia, he was also seeing other tumors being produced and it was obvious, just talking to him, that he had another virus with these polyoma-like tumors.

The way he had gotten that newborn mouse trick: apparently he had been inoculating mice, and I don't know that he was having that much success right off, but he happened to have some inocula left, as I recall, and he said he had this litter of newborn mice, and he was ready to home and he thought he'd inoculate the newborns, and bingo, they were

the ones that really came down with leukemia, and they settled the issue for him of cell-free transmission.

There were other people, like that group in Steven O. Schwartz's lab., in Chicago, who were talking about having a transmissible agent, transmissible by inocula, and he was publishing in *Proc. Soc.* But, just looking at his pictures you realized it was inocula of cells; it wasn't cell-free. I don't know whether I should say this here, but it was determined really that he had a very helpful technician, and it kind of blew up there and she went for care or something or other afterward.

Baker: Grafe, I guess, added to the information here about this time?

Manaker: Yes. I think so. In Germany?

Baker: Yes.

Manaker: The Russians were publishing too, you know, and they were getting success by putting stuff from humans into eggs and then into animals and the rest of it. I was never really sure about this whole thing.

Baker: Was this Zilber?

Manaker: Zilber, and there were others involved in there also. And somehow or other, considering the climate there, one is not sure whether all of this was manufactured, or whether there was anything real in it, but it just seemed odd to go from human to egg to some other animal--was it the monkey--and so on. But, you know, it did set something going out there in those Sukhumi monkey holding areas, you know, where that-- Oh golly, what's his name? We used to go down there and visit him in Sukhumi. Do you remember him?

Baker: Yes. I remember. Boris Lapin.

Manaker: But he had something there. It's just that I guess he sent some animals here to NCI, and I don't know that there was anything that came up out of the ones that he sent here from his group. But certainly we saw pictures of some of the spleens and things from some

of his animals indicating that it was for real. And this was following inoculation from leukemic humans, introducing the material into his monkey colonies. So they may have had something there; it's just that considering the climate between our two countries and considering what conditions they had to work under there, I was never really sure. But this is just between us. At least I wasn't convinced.

That gets us down to Gross and his polyoma and his leukemia. And then sarah Stewart and Bernice Eddy, certainly, here. They got in there and characterized a polyoma-producing virus and, I think, carried it right on down. They knew what they were about, you see, whereas Ludwig really did not. He was out of tune to it. And they could very well leave him in the dust.

Baker: Well, a lot of people didn't believe Sarah Stewart's findings too. Didn't Dr. Mider ask you to also do some work along those lines?

Manaker: Well, the reason was that she was getting all of these tumors with human inocula. But, you know, I don't know if you remember Building 6 in those days. It was overrun with roaches, and I know I ran into that trouble too.

Baker: I know that. Building 6 was where I started at NCI in 1949.

Manaker: Yes. She had-- And I'll tell you, you'd go in there at night and turn on a light in an animal room and the benchtops are all black with bodies. I don't know where they all go considering that there are tile floors and things, but they disappear like that.

Baker: They've been around for 3 million years unchanged. You know? They're pretty clever.

Manaker: But it was a problem. It was a problem to me too because I had set up that cell line, you know, a long-term producer, which would have frozen Moloney's virus. You see, Moloney followed the procedure that Ray Bryan had set up with the Rous virus, picking the early tumor producers, passing that, and so on, and building up, let's say, the potency of his virus--or virulence, whatever you want to call it--but Moloney, in doing that with his murine leukemia virus, was getting it to produce leukemia earlier and such

stuff, but one was not sure what his final virus represented. You see, the virus does change. It does pick up things and so on. And, considering the nature of these bugs and the fact that they had pretty well disseminated within the animal colonies, it certainly must have altered his virus over the period of time that he passed it animal to animal.

I felt that in getting it into cell culture and freezing some of these cells from newborn animals in cell culture that we could perpetuate it, and one could go back to the virus grown earlier. And it would have been great if, at that time, we had had liquid nitrogen, but we didn't have the funds in the area and we just didn't have liquid nitrogen storage. They did at Huebner's lab., but we didn't have it. So, I was out of luck.

Anyway, eventually the line was lost because there was demonstrated a contamination with polyomavirus, which apparently could only have come on in from an infection of the mother who bore the young, or the young there in the cage probably from Sarah Stewart's polyoma studies in the same building carried in by roaches as they'd go from animal box to animal box and such.

Baker: Did you ever publish the idea that the roaches were involved?

Manaker: I didn't publish that they were, for I couldn't prove it. But I don't know how else they would have gotten in there, because I don't think that one would have expected polyomavirus to be so widely disseminated within the animal colony because I was using BALB/c strain mice and they were a pretty good strain of mice. I didn't observe anything coming up spontaneously in those animals and, you know, I kept animals--quite a large number--for a few years checking out Sarah Stewart's contention that brain extracts from human leukemic individuals were producing this multiplicity of tumors, which was contamination, naturally, in her animals.

She was following Steven O. Schwartz's work in Chicago, you see, where he was indicating that he had immunological suggestions that he gotten something from leukemic individuals into guinea pigs, or into some other animals, or into mice, and that

brain extracts of leukemic individuals were effective. And she was using brain extracts and coming down with these polyoma type tumors. But it was only because of cross-contamination. And how the cross-contamination occurred, I really don't know. But I know that in my lab we didn't get that kind of multiplicity of tumors, and we had, oh, I guess, about 45 percent or so of all females showed evidence of large spleens and stuff--things like this--at the time of death, holding them until death and then posting these, but there was no evidence at all, as far as I was concerned that I had anything regarding tumor induction. I had two controls for every test animal. That is, two control litters, two control mothers, to every mother and litter that was inoculated. And, examining all those animals indicated that, sure, there was an undercurrent of some kind of a lymphoid disease that goes in there, but nothing suggestive at all to indicate that human materials inoculated into baby test mice had anything at all to do with what they were experiencing. That is, controlled animals had the same incidence of splenic or node involvement such as did my test animals. No difference.

And that occupied me for a long, long time. We gave it the good old college try. And I was very, very interested in this whole business of human leukemia. But I'm getting away a little bit from some of these other people. I had mentionedGross, and we mentioned Stewart and Eddy.

Stewart and Eddy did fine and dandy when they were working on the *polyomavirus* in mice, but then things got a little bit more complicated. There was not enough there for two people working in mice; so Eddy decided that she was going to go into hamsters. And I was chatting with her and she said, you know, she was doing all of these studies with these monkeys on this program of Salk's vaccine and such stuff, for the Vaccine Program on poliomyelitis, and she got normal kidneys coming on into her lab for tests, and she said, "Well, why not take some of the normal kidney extracts and shove them into hamsters?" It would give her another route, other than the thing where they were

running and butting into each other on the old polyoma studies with Sarah Stewart. So, she did. And she ran into something that she called, I guess, a lacy virus at the time. And eventually I guess the people up there at Merck Company, at West Point, Pennsylvania got into the activity. They hopped on that the minute they heard about that. She reported results at a New York meeting--the paper--and they hopped on it, and they indicated, well, this virus was SV-40, and so this is the birth of SV-40 story. I know that Dr. Smadel was sore as all get-out about her publishing that and he took her lab away and he ended it all, took her technicians away and such stuff. She resented it deeply.

Baker: Did you get involved in that?

Manaker: I sure did not. I sure did not. Anyway, the poor lady-- But she really was a nice woman, and she got in there and did something. You almost had the feeling that a hamster would turn over with a tumor no matter what you gave it after a little bit. And then, of course, there was Moloney. I don't set as great a store on his murine leukemia virus as I do on his sarcoma virus, which again crept up and was a nice adjunct to the overall program. And I think that's a noteworthy area. It was surprising on that sarcoma virus. I tried propagating that in cell culture. And I would hold these cultures for about a month and I didn't see anything. I was using BALB/c mouse monolayers and I never saw any suggestion at all that I was looking at a cellular effect. And after about a month I began getting the leukemia coming through, and my inocula in animals showed the disappearance over time of my sarcoma activity and our leukemia coming on up bringing animals down.

And it's surprising that Wally Rowe got it. You know, he got a sample from John Moloney long after I got mine. But whether he put his into Swiss strain mice and there was a difference, or whether it was the fact that I got mine a little bit early and he got his later, or he had something else I didn't have, where he was getting transformations,

but he did, and I failed. It wasn't that I didn't give it a college try. I worked a year on that blessed thing and it would always fade away.

Baker: Well, this illustrates again how, before you understand the way things work, how complicated the tumors can get.

Manaker: Right. I want to discuss the Epstein-Barr virus. That was very, very important because I think that the overall exploration of that herpesvirus cost us a lot of money over the years, and I understand that that virus, put into a marmoset (I think it was a cotton-top which I guess was one of those bad species to try to work with, but usually couldn't get anything) induced was a B type lymphoma which was, as you know, suggestive because Burkitt's tumor was the B type cell. And beyond that I don't know. It rambled around. The Henles took a hold of that virus for a while. They were lucky. They had a girl in their laboratories, as you know, who was negative and they used her sera as a control. Then, all of a sudden, she got infectious mononucleosis and her serum became positive, and they made their big study of college students and so on and came out with the infectious mononucleosis relationship. And I guess that herpesvirus is blamed for a lot of things, but it never really materialized into an awful lot. But I think it awakened that whole business with herpesviruses and herpesvirus Type II in cervical carcinoma and all the rest which, to me, I thought quite weak. Some of the areas where you had very much tumor involvement and such stuff in Africa, didn't jibe with some of the South American studies. I kind of forget a little bit about this but, in my own mind, I didn't think that there was anything too conclusive there.

Baker: Did you get involved with the African adventure?

Manaker: Well, the way I got involved in that--Epstein-Barr--we had-- Well, first of all, we met Epstein, you know, and he gave us the story about looking at this stuff and seeing this herpesvirus electron microscopically, and then we got a visit from our friend Pulvertaft who had in his breast pocket some test tube cultures from different individuals with

Burkitt's tumor. And I looked at them and I think there were 9 or 10 of them--

Baker: These were cell cultures?

Manaker: They were cell cultures. And one of them, the best producer, Number 9. I named it "P" after Pulvertaft, P9, and we gave that to Pfizer, who produced it for a while. And, as I say, it was the most consistent producer--others were sporadic-- but this one was good. And that was then a production effort. So that became available, and I think it was important to think in terms of providing that to people who wanted to study it. You know, there was a *Herpesvirus saimiri* virus that crept on up from a squirrel monkey which, I understand, also induced a leukosis in a marmoset. And that sort of kicked around for a little bit. I know I had tried to prompt one of the people, Vandervoot, in our lab, to work with *saimiri*. He was working with the herpes Type II virus. And he indicated that, while he might have introduction of the virus genome into cells, that it always was a plasmid type. He didn't think it ever incorporated into the genome, the way one would expect with the retroviruses. So, there was a difference then, if you go along with that. But I couldn't get him interested in picking *saimiri* virus at all. Then of course if we're looking at something important apart from Epstein-Barr, Moloney, Eddy and so on, then Huebner and Todaro, with their oncogene hypothesis was really sort of hitting the nail on the head. I imagine that comes on later.

Baker: Yes. It wasn't quite right, but it stimulated the thinking.

Manaker: Yes. That's right. And, in fact, I think this whole program, even though, as I think in your questions you mentioned that, did everything in the world to stimulate peoples' thoughts, ideas, working, and gave them tools, gave them materials, so that if they weren't interested particularly in the human viruses and such stuff, *per se*, there were a lot of ancillary activities that went on. The simian virus-40, for example, coming out of there, provided genetic information because it was a rather small genome. You can get in there and work with it. And some of these other things. The reverse transcriptase

production down there in the Florida laboratories, providing this material to people working up in the various labs here--our own, right here at NCI--I think was a godsend. These things were really quite important.

So, that just about covers it, I think.

Baker: Did you ever visit the unit in Africa?

Manaker: No, I never did. I almost had an opportunity to. Dalton was suggesting I go along. But he changed his mind, and I didn't get to go.

Baker: Yes. I never got to go either.

Manaker: I never did. I understand it was a beautiful country. And that was so tantalizing because, as the story came on down, above a certain level where there were few mosquitos you didn't have the Burkitt's tumor. You get on down a little bit, down lower, where there are mosquitos, you get Burkitt's tumor. Because you get this herpesvirus in there was a red herring, I think, as far as Burkitt's tumor itself was concerned. I don't think it really had that much to do with it. I just think that what it was, was a virus that happens to inhabit quite a number of people roaming around this country, as well as the Africans, and that probably is transmitted as a "kissing" disease, as infectious mononucleosis, in young people. It apparently does not do anything to children, very, very young children, but it affects those that are teenagers. And whatever is involved in Burkitt's tumor certainly must be related to maybe an insect vector. It has all the earmarks of an insect vector-borne disease. But, beyond that, you can't go, and at that time the political climate in Uganda was not very good either. It's one of those things.

Baker: Are you satisfied that the Epstein-Barr virus is a causative factor in inducing Burkitt's lymphoma?

Manaker: Not really. It might be. Gosh, who can say? But it is a virus that is apparently so widely distributed that it makes you wonder whether you would not see that kind of a

disease much more frequently than you do. You know, it seems to be localized in specific geographic low-lying areas. My understanding is that individuals, who had previously been free of the virus, now move into lower areas where they might be bitten by mosquitos, are the ones that may come down with tumors. And it doesn't have to be in youngsters either. Older individuals may come down with a Burkitt's type tumor too. It's really worth a lot of investigation, I suppose, and maybe if it were more important, other than a disease involving a small area, that maybe much more effort might have been placed on it. I know that we did an awful lot of probing and so on with it.

Baker: Is anybody looking at the genetic code sequences in that?

Manaker: You know, it's such a big genome. The herpesvirus is a difficult one. I'm not sure about this stage of it because right now, if you wanted to pick one, pick a human virus; it means more. But, on the other hand, at that time people were looking at something that was realistic. That was looking at something like the SV-40 genome. It got to where you knew what you were dealing with. You had the whole thing.

Baker: Yes. It was much easier to unravel.

Manaker: Yes. You could work with it.

Baker: Okay. That's a good account for the first question, and you touched on some of the others, but I'll ask you the second question again. What do you think the key administrative or management decisions were and who made them, as you understand it?

Manaker: Well, you know, I always go back to Mider, probably because he was the individual I met there and probably was also the one who was responding at the time, with yourself, to what was going on. I understand that Wendell Stanley had made quite a speech about something needing to be done in this area.

Baker: Yes. He was a very crucial one before the Appropriations Committees.

Manaker: That's right. And this thing started the ball going. And I think the people at NCI that

were receptive were important.

I wonder if I could digress here a little bit and tell you some of the things that bothered me a little bit at the time? I worked together with Meryl Stanton quite a bit--he was a nice pathologist--but he never believed that any tumor was produced by a virus. For example, he thought that the polyoma tumors, or the leukoses, were not real tumors. And I asked him, as a pathologist, looking at this, "Can you tell me how I could discriminate?" He could not tell me on the basis of pathology. But, you see, this is how he felt, because this is what he was taught.

And I remember Thelma Dunn going off to a meeting out there in the southwest part of the country, and I read her presentation in one of the journals, and she had looked at Moloney leukemia, had studied the animals inoculated and the occurrence of the disease, and she said, "Well, I cannot believe that this disease is provoked by the virus. I would be far more willing to take for granted that the destruction of cell material and cellular debris would be provoking the cell changes, rather than a virus inducing the tumors. The debris would provoke the change." But, you see the misunderstanding? No one understood then that the viral genome gets in, and the viral genome does things. The perception was not there. And so, for a long while there was this kind of wall.

Baker: Well, of course Ray Bryan fought this and kept--

Manaker: For a long time.

Baker: --kept the flame alive, while this view was very prevalent.

Manaker: Do you know the sorry thing was he picked the Rous virus and, of course, the Rous virus kills the cells. You and I know it. And it was one thing that you would never have dared to even mention to him. I think he probably would have exploded. But it does. And it is admirably demonstrated that if you take the one kind of tumor, let's say from a male, and put it into a female and it can become a female tumor and the male cells disappear, and such stuff. And I know in cell culture the virus kills the cells in the

culture eventually. They hold on to them and they die. It's a destructive agent. So, I'm not really sure that you can call it a real kind of "cancer" virus. It causes proliferation more than anything else, wouldn't you say?

Baker: Well, you have to describe it in detail and then you worry about giving it labels. We think we understand things when we give them labels, you know, and so people at that time, particularly the pathologists, had trouble giving that a label as a--as they called it--a "real" tumor. Of course, "tumor" literally means swelling, so I don't know why they didn't say a "real cancer."

Manaker: I think one of the other difficulties at the time was this: a lot of people had their programs going and they were important to them--genetic studies, all other kinds of studies and so on--and suddenly to have a whole new discipline, like a virus oncology discipline, thrust in (and particularly a discipline where one really didn't honestly believe that maybe this was all kind of for real, but it was just getting a little bit too much attention) led to an understandable rebellion of kinds and a kind of shying away, and a little bit of a cold shoulder to some people who were working in the field. I think that this sort of hurt a little bit for investigators who were in it who maybe got enthused about the whole thing and maybe felt that there wasn't enough sympathy--you might call it that--for them. The other thing now that we're coming to this business of the administrative and management decisions and so on, was the fact that these people setting up the Program had to counter this attitude. There were people in the field outside the NCI who were thinking that the Program would be large and were wondering how it would interfere with what they were doing and take money that was coming to them. And also, when you start setting up a new program with frequent reporting of results, people begin getting edgy. They don't like to give up where they're going. It's hard enough to get into research and define an area of investigation, to get on in and hope you're not scooped and so on, without getting in there a loner and beginning

to breeze around where you're thinking and what you're thinking and where you're going. It's a very difficult thing to do anytime--I would think, anytime-- particularly with a "Contract Program" and one like the Special Viruses and Cancer Programs. And a "Grants Program" gives a considerable amount of personal liberty. The "Contract Program" in welding something into a unit and figuring that you would have people who would get together, exchange ideas and work together and so on, and suddenly become, oh, just like development and not research--no, this is not an activity like that of a scientist.

Baker: Yes. I'm well aware of this point of view. But it seemed to me we needed both kinds of activities.

Manaker: Well, you sure did. You sure did. But this was one of the headaches that one had. If you could get together, just as you did on sending people to the Moon, on having some embryo people write up a computer program--can you imagine writing up a software program to go to the Moon, go around that, and come back?

Baker: I can because I read the original plan of the Space Program.

Manaker: Yes. Those guys that wrote that were sweating, I'll bet you.

Baker: I'm sure.

Manaker: Anyway, so what do I think were key administrative-- Well, I really don't know very much in there about that. I could say the people that I knew, yourself and Rauscher and the other people from inside, and who helped make the decision getting it started, the input of Rauscher and Carrese in developing the plan and such in there, were all the people that struck me. But, you know, behind the scenes there had to be other people who were the people who really counted to make it go. That would have been like yourself, maybe Bo Mider, maybe other people outside that I wouldn't be aware of.

Baker: Not Bo Mider; he was very opposed to any kind of planning in research programs. You remember the special request for $10 million dollars?

Manaker: Yes.

Baker: Endicott was a key individual in that because he accepted our recommendation that this program expansion be done, and Ray Bryan, Dick Rauscher, and I, with Zubrod also reviewing it, prepared the documents which were sent to Shannon. So Shannon had to approve Endicott's being allowed to go and ask for the $10 million. And so we wrote two documents justifying why we thought it was worth seeking this Program and the funds, and Shannon bought that. And so those are the administrative decisions that I consider very critical.

Manaker: What do you consider to be the main activities and effect of my participation in the field during this period? Oh, I don't really--

Baker: Don't be too modest now.

Manaker: All I know is I got involved in this and in short order it became quite obvious to me that it was impossible to do much in the lab, and this is one of the reasons that I didn't. There were telephone calls always. I think Dmochowski from M.D. Anderson Hospital in Houston was on the phone all the time. It was really kind of rough going. I had a couple technicians and I had this program going, you know, looking at human leukemic materials, and I had tried hard to get normal human materials, generally from people who were undergoing--children in particular--undergoing heart surgery. And I could get ribs there and strip them free of cells and get cultures going. And then Ray had gotten together with Jack Dalton, and he had assigned a gal, Artrice Valentine, to to take a look with me at some of the samples that I would have to see whether we could visualize any virus particles. After all, in those days there was no way of testing to see whether one had anything there except visually. You didn't know anything else. Serology with what? How? There may never be anything there. If you could see something that you were propagating, I think that would be the first step. And it seemed to me important to get something in hand that you were propagating, something

where you could maintain what you had, not to take a quick look and then it's gone.

Baker: Well, certainly the electron microscope helped move this field along, but I felt they never had adequate controls.

Manaker: No. I never got the kind of support I needed. I spent sometimes maybe 6 weeks nurturing, concentrating, fooling around with cultures, trying to sweat something out, and have the girl mess it up. And it happened over and over again. And, after a little while, you know, you begin to feel, well, maybe there really isn't anything there. But then, look, our good friend Gallo turned it up and the French have turned it up. It was there. It was just-- I wonder whether or now we gave it--or the people backing me there--gave it the old college try, but I'll tell you right now I sure worked like a beaver on that aspect of it. It was really quite disheartening.

Baker: Did you feel considerable regret that you were finding it difficult to have time in the lab?

Manaker: Well, pretty much. I'll tell you, the world was changing also. You know, right about that time, the old school and the old animal business--you're putting things into animals, you're watching animals come down with disease, you're passing things, you're going through Koch's postulates, you're doing all of this kind of stuff--I ran my thing with that liver pathogen that I found in there, the hepatitis virus in mice. I was desperate to get something out. And when I ran across that thing coming across in my cultures and the fact that it would destroy the livers of baby mice following inoculations, I just followed that thing through for what it was worth. I looked at the mothers, demonstrated that the mothers provided immunity in the milk so that they protected their young even after the inocula, that the adults didn't come down with it, the babies showed it, the way it finagled around. In fact, I gave the write-up for publication to Wally Rowe to review. He thought it was a really quite good paper, an excellent paper. He said it was an important thing. But, you know, at the time, Ray Bryan had sent my paper up to Joe

Smadel. Smadel called me in. He dragged out a paper from some fellow in Japan who did a Kottner fixation study on some hepatitis in mice there and said, "This is the kind of paper you ought to have." And all the stuff I had showing how you could titer this stuff, that the results of titration performed to the Poisson distribution, that you could deal with it and titer it and the way it behaved in animals and the way it affected the adult and so on--what it did--was beside the point. I felt devastated. I went back to the lab. I derived some viruses from people out in the field and ran Kottner fixation studies which showed that mine had some differences serologically from theirs and pushed that thing through and published it, so at least I got a little something to show for all the work. But I was desperate for something to do to be productive. What really, I'll tell you, I needed was an opportunity to get, as I did after a while, some outstanding staff. When I got Khoury into the lab and Vandervoot in there, who built a nice lab. Khoury really had a beautiful lab. And I went to work in his lab for a while and did a lot of these DNA studies and, you know, the sequencing and such stuff, in his lab.

Baker: Those were important people to get there, weren't they?

Manaker: I got a publication out on some of this stuff on enzymes and the other things. But I had come out of the old school, the other school, where we had animals where we inoculated viable eggs and looked at destruction, or animal activity, or animal convulsions of one thing or another. Well, so did Rauscher. We were oriented this way.

Baker: So you're making a point that the whole approach shifted about that time?

Manaker: All about that time. And it would have been wonderful if you had the--

Baker: And that's part of this laying the foundations for molecular biology.

Manaker: Yes. And if, at that time, as a young investigator, I'd had an opportunity to go into someone else's lab to pick that thing up and come on out and set up shop it would have been wonderful. It would have been wonderful though to have had the opportunity. And I think for any investigator to be able to grow by being able, in his own niche, to

move out of it for a while and spend some time in another active laboratory is extremely important. Am I rambling on too much?

Baker: No, no. This is wonderful. It gives me a lot more understanding too.

Manaker: Well, you see, being a rather senior player in the Viruses Cancer Program, suddenly you find yourself exposed to a lot of other individuals who are actively working in an area in which you have a keen interest. They also are providing information of sorts to the overall Program. You're much more aware of a whole field of investigation. I knew more about what was going on in every corner of this field of investigation than ever before or ever since. It was a wonderful thing. And I think too that you needed someone who had a background in this area so that he could also use his judgment about the selectivity, or what was happening, when, and how important it might be. I know, at the time, there were things going on in laboratories where I actually took a trip and visited with the laboratory because I thought that they might be able to provide to the Program, and tried to talk the people there into maybe putting in a contract request to see whether or not they might not become involved with us and use some of what they were doing to help bolster the Program. A lot of the folks felt that it would be just too much for them; that they had little labs, with few people. Well, we said, "We'll give you a little bit more, and so on, if you need it." But, no, they didn't want to. It was very hard to recruit people coming in. And I think if one is looking back, one of the problems that is involved here is that after a little bit you become so dependent upon the input, e.g., someone coming in with a request for funding by a contract, and some idea. And this could go to a review group, and sometimes a review group agrees and sometimes they don't. And in this respect it's almost like a grant type operation. What I thought was lacking and what I hoped that we could have had, was an internal group like a think tank. With an external group, you couldn't sequester the ideas and the time and the thoughts of the people out in the field to do the kind of think tank work that you

really wanted. But I thought that within the program, if there were a think tank arrangement made, where you had a group of people who were kicking around what we had, were thinking about it, and were--

Baker: Well, I thought the committee chairmen constituted such a group.

Manaker: In a sense they did, but not to the point where they got together in a business-like way and said, "Well, let's do this." I thought that there was an awful lot of lonesomeness out there. Bob Huebner did what he thought was important to him, following along his polyoma studies in wild mice, and in going along with the CAT and the other things out there, and he was an entity in his own right. This was his. And other people-- And you feel quite alone. I felt quite alone in my bailiwick. I really did.

Baker: Well, from my level, I looked upon the committee chairmen to provide that function.

Manaker: Well, you know, we had our meetings and such stuff, and generally there was a review, and I was so disappointed to hear from a number of people. One of them was Skolnick who said, "You know, I feel kind of funny here thinking in terms of people who probably know far more than I do out in the field and sitting in judgement of what they're suggesting and what they want to do." And that's not it at all, you see, because what you want out of an individual sitting around at our meeting was not the feeling that he's sitting like a judge about anything, but to take what's there and maybe begin to open it up, tear it apart, for visualization, for look at the juicy, good, important parts of this kind of thing, so that it could be built on.

Baker: It's a hierarchical thing like an organism. You're talking about putting together this stuff out in the field at a higher intellectual level and now looking at where do you go next.

Manaker: Yes. And that, I thought, was lacking: where do you go next. You put your finger on it.

Baker: I didn't think it was earlier, but, as a matter of fact, the planning that Rauscher, Carrese

and I did for three weeks was that kind of think tank work, and then we looked to the committee chairmen to try to continue that.

Manaker: You see, you're looking at what is needed in a broad sense there, and I think that you could see, right now, looking at the AIDS virus, the significance of being able to manage it in a laboratory, to think in terms of can you do trial studies for vaccine production, or chemotherapy, or one thing or another. Do you have something in hand? Do you have an experimental animal that would be wonderful? You know, this sort of thing. You're getting a grip on the agent, where you're managing the agent. You can put your hand on it. It's in a test tube. Do you see what I'm driving at? And at the time when we were there, you're looking vaguely out there. "Is there anything I can put my hand onto, to get it in and, if I do, and I suspect it's there, how do I get it into the test tube, how do I get into my laboratory? How can we begin to actually handle it, work with it, come back to it, make it, dispense it?

Baker: Well, as I said to Bob Miller, when he kept milking the scientific literature for epidemiologic studies, I said, "Bob, you do a great job in finding stuff that's already there. What do you need to do to go out and generate what's not there?"

Manaker: Right. That's it. That's a significant thing. Right.

Baker: And I think it's not only reaching out there in the field and grabbing something; but what is not there that ought to be there? And that's what the contracts, I thought, could do better than the grants.

Manaker: Well, you know, we, sitting in that contract review--

Baker: But you're telling me that didn't work as well as you had hoped.

Manaker: Not as well as it could have. And I'm not sure whether one could say that it was attitudes or whether it was just that the decision to go ahead and actually mount it in this way. You know if we sit here and have a B.S. session, we have nothing more than a beer right here and so on, and we begin to say, "Well, here are things that we know.

And, you know, this joker came on in here and he had a little something. Do you think he's got anything there and, if so, could we use it someplace else," now we're really working because now we're getting together and we're talking in a very, very close peering-into-it situation. Whereas, if you're at a meeting and you're thinking about doing this, and you're being a little bit more formal about it, and you're really looking at it with the point of view of "Does this guy have anything here? Is it going to be worth the money? Should we give him this much?" and we're at a different level. Do you see what I was driving at?

Baker: Yes.

Manaker: Yes. It's a different level.

Baker: Well, I guess I assumed the informal stuff went on maybe more than it did.

Manaker: Not as much as it should have. I really don't think so.

Well, there was another disappointment I had. For example, here we have a fellow named Khoury. Now, he's a very bright person. I understand that he had a 145 index--what do you call it--intelligence index.

Baker: Oh, IQ test?

Manaker: IQ. 145. That's really up there. Anyway, more hats off to him, but he sat in at a meeting and I told him, "Why don't you come on in and attend our meetings and contribute to them?" We were talking, I guess, about some kind of a study on human breast cancer as a contract area. And he says, "Well, I don't know anything about that," and in a way he thought he'd be wasting his time. And I suppose he's right. He has only so much time. He's got to think in terms of where he's going and what he's going to be doing. He doesn't have any time to fool around with the Program activities. That's the other way of looking at it, you see. But a disappointment, because here you have a bright individual, and maybe he could have contributed effectively. And so now what we're looking at are the two different things: the man in the laboratory who has to

work about, think about, it's publish or perish, and not just publish or perish, but establishing his name and his standing in the scientific community. This is what you call power. It's a power, not just a money power, but a power of an intellectual kind. You're recognized and respected because you now know the area and you're in there. And these people all reach for that. And this is why it's so difficult, in a way, to say, "We're going to set up a Contract Program. Let's get people working together. Let's all join in." No, no, no.

Baker: It's very hard. Yes. I know. But again, do we need both, or not?

Manaker: Well, I guess we do. You sure do. Absolutely. And the point is now, how can we weed out the people who don't want to do that? Well, maybe it turned out that a guy like me, who was working in the lab and then got on in there and found that I could find some happiness in just knowing what's going on and so on, and working in this, is just as important perhaps. And maybe that was my contribution to the thing.

Baker: Yes. I think that's a very important part, a very important part. Yes.

Manaker: So let's see, we were--

Baker: Well, I think we answeredQuestion Number Four pretty well. Let's go to Number Five.

Manaker: I was not that aware of the outside advisory committees, like the National Advisory Cancer Council or Board, and so on, and the meetings there, since I never had much of an opportunity to get in and contribute and do things there. But, insofar as some other Committees went, I think that as far as my own outside review Committee, I tried to get the best people we could, and we really had some good people. I tried to get representatives of a number of disciplines. I happened to recruit this guy from England, no less. He didn't want to come on over at first, but he did after. A good pathologist. And I think after a while he moved to this country. And I'm trying to think of his name. You know? But, in any event, I had pathology represented by--

Baker: Who kind of stands out as most helpful?

Manaker: In terms of?

Baker: Getting on with the job.

Manaker: Well, my gracious sakes, in terms of review committees, well, we had M.Ds., pathologists, and virologists and so on, on my particular review committee, and I can't say that any one was better than the other. I could give you one example of what kind of help you get from this. There was a guy who was interested in the bowel. What the devil is this disease where you have these lesions?

Baker: Crohn's?

Manaker: Crohn's disease. And he had a feeling that perhaps a salivary gland virus--maybe it was, I don't know--might be involved in Crohn's disease, and whether or not also there might be some predisposition to developing intestinal cancer as a result of this infection and this activity of this virus, so maybe it might be an important area of investigation. But, in any event, he submitted a proposal for a contract to help him out, and he was going to have any number of members of his staff that would succumb to it, as controls to having these--what the devil do you call them, it's on the tip of my tongue--

Baker: Fiberoptic proctoscope?

Manaker: Fiberoptics going up in there. Yes, the proctoscopy, to examine their colons as controls. And then he would be looking at a lot of patients that he had with Crohn's disease, and it might make a worthwhile study. We brought that up for review and our people on the Committee said, "Do you know, this is a danger. He may perforate the intestine with doing that proctoscopy."

Baker: That is a risk.

Manaker: Yes. And other things. "And who would want this?" So they negated this. And, in a sense, having experienced people on the Committee who could pick up Questionable items was valuable. Just that this would be just one little example. They came on the Committee with diverse backgrounds and thus could contribute substantially to most

kinds of effort you might begin to envision. So I thought they were a wonderful group and, in fact, they were all pretty well respected out in the field.

And a guy like me probably might feel a little bit nervous with a group like that, but I think we got along pretty well. The other thing that we had was a pretty good group of internal groups and committees. At first hand I know about that. On the other hand, when I think about our internal committees with the people there, I wonder whether the internal groups, on the basis that I have already spoken about, maybe we didn't have enough planning and informal discussions from the internal people, and maybe there are other things involved. I know I spoke a couple of times against some programs, one of them in Africa, that was suggested where I knew doggone well this guy just wanted the money to go fooling around. And I don't mean that personally, but the guy over there, and I didn't think we'd get anything out of that. It was a human breast cancer study of some kind. But, on the other hand, it passed. Other people thought, well, it was worthwhile. I just feel that maybe sometimes there wasn't enough in-depth thought and in-depth consideration about funds and money, and the rest of it, and what was worthwhile.

Baker: Do you have any impressions of political figures that were involved here?

Manaker: Nobody politically ever bothered me about anything. No. Really. Political pressures?

Baker: How about the other way around, the support?

Manaker: Oh, well, that's true. I would rather hope that we had-- Certainly, I guess Nixon was right on in there.

Baker: For all of Mary Lasker's problems that she gave people, she was certainly influential here.

Manaker: She certainly was.

Baker: And Sidney Farber.

Manaker: And I guess Benno Schmidt certainly.

Baker: Well, that came later, later than we're talking about right now.

Manaker: Yes. He did.

Baker: Okay. The sixth question deals with resources.

Manaker: You know, that's terribly important. I don't think that there is enough thought given to the resources. But when reverse transcriptase became important and larger scale production of it permitted its introduction into the laboratories on a broader basis--I mean not just of necessity in a Program laboratory, but to maybe other laboratories where things that might be important to the Program were going on. The larger production of reagents provided a new opportunity to get some of that material as it was made available. I know even in our own lab with Khoury it was terribly important to get some of that material for the work that I did in his lab depended on it. So, yes. I think that that was important. Tissue culture cell lines. The opportunity to get human kidney cell lines, or human fibroblast cultures, things like this. If you have a smaller laboratory, you can't afford to go out and buy much of anything. If you have an arrangement--

Baker: Well, they weren't even available to purchase in those days.

Manaker: Right. They weren't. I remember when I got out of Huebner's lab. You see, I came over, when I first joined the place in NCI, a lab for me was not available, and I worked over in Building 7 with the Huebner group.

Baker: No. I didn't realize that.

Manaker: Absolutely. For about a year. And I got to know him pretty well. And I know that they would get human embryos from downtown. They had an incinerator and they'd get rid of these things very quickly, you know, and whatever was left over they'd get their different organs that they had. They could set up their fibroblast cultures. They had a good set of technicians in there that would run the whole thing through. They had a technician that was knowledgeable in serological studies and the rest of it. And, you

know, when I moved over to Ray Bryan's lab, we had nothing like that. We had no immunologist. Nobody that you could turn to. Over there, I was accustomed to getting in there and watching these people. When they were doing serology they got antisera all over the place. So, I'm glad I was there because I got a wonderful education. I sure did.

Baker: Well, the old-fashioned virologists really knew how to work together, even though they were competing.

Manaker: Yes. When I actually move over I had my antisera and my other stuff and so on. That's right.

Baker: When I told them that the trouble with their activities-- It was great that they checked each other out on quality control, but by the time they sent it around to each other they'd used it all up, and that's why we wanted to make bigger batches industrially.

Manaker: It was important.

Baker: Well, they said "The industry people won't be able to make it good enough."

Manaker: Well, I wouldn't say that.

Baker: Well, I said, "Test it. If it's not good enough we'll throw it away. But you guys use your stuff all up. We need more of it."

Manaker: That's right. One of the most important things going.

Baker: And that, I think, was a very important element in the Program.

Manaker: You bet. That whole Pfizer operation with the ability to kick out larger amounts of virus preparations. In fact, the fact that Ray Bryan was kicking around and sending around Rous virus, you know, in the early days, probably did an awful lot to get things started here or there.

Baker: Yes. It took a lot of his budget.

Manaker: Yes. It sure did.

Baker: And he had so little budget--

Manaker: You know--

Baker: And time. He spent a lot of time on that.

Manaker: Yes. I know what Bob Stevenson did in the Grants Program in supplying things. I know. I tried to glom onto some of his stuff. It was hard to get stuff. Anyway, you know, I was lucky. I managed to get-- I had some friends, some guys, that worked in my lab for a while, the M.Ds., for example, went over to St. Elizabeth's General Hospital downtown and they would provide me with some embryonic material. And I had a guy in Indianapolis I knew from Rutgers, and he sent me some material. I even had this fellow Ito that we had over in Japan send me a little bit of something at one time. So, that I managed to get a little bit of material like this. But eventually what you did is you end up buying monkey kidney, and the price was horrific. To do any kind of a study was expensive. Do you realize how much it cost to do a study in molecular biology where you're getting, let's say, SV-40 virus and concentrating it down and then getting a genome from that? It's $40,000 dollars for the shot. I used to think, "My God, that's more than you'd pay for a house," back in those days. That's a lot of money. And that's really just too much. And I'm sure that if one could have had a good set-up, could have overcome the religious and other legal and other barriers against it at the time, that maybe we could have gotten good material coming in, because the kind of stuff that I would get, if I got something, let's say, from my friend, was something that you'd wonder about, because you'd take a look at the embryonic material and it had lesions all over it from some spontaneous abortions and other things. Bob Huebner had some very, very nice material coming in, and this is the way he could keep going over there in that lab.

Baker: Well, part of his skill was setting up these linkages.

Manaker: Sure. And Sarah Stewart did too. You remember that one?

Baker: Well, that's all part of the game.

Manaker: It was wonderful.

Baker: But at least, when we produced large quantities of some of these things, it overcame those restricted sources.

Manaker: And you could begin to see, yes, the importance of having it.

Baker: So the whole field could move.

Manaker: You know it. Anybody. Every little guy.

Baker: So I think this set the stage for biotechnology.

Manaker: Terribly important. All of that work. Yes.

Baker: Well, Question Number Seven, you may not have much grasp of how much money went into each area.

Manaker: The grants and contracts, I never really concerned myself too much. I know that the grants people always seemed to feel that something was being taken away from them by the "Contract Program" which was absolutely erroneous. And I know that they had as much freedom to get in there and really be contributory, and stuff, in the "Contract Program", and there wasn't any opportunity for their stuff to be stolen or disseminated, or whatever, information that they might have to contribute. I don't know what they were afraid of. But I want to tell you one other thing that was very obvious to me, and that was that there was an awful lot of the money that was in there that funded an awful lot of other little things in other departments and stuff out there. It wasn't all going to ardent investigative stuff. It often came in departmentally and maybe it supported a little bit here, there, and in other places too. So, I think maybe it was a little easier to do that with grants than with contracts.

Baker: Well, I think there was less accountability in a detailed sense.

Manaker: Than in contracts. Right.

Baker: Number eight, you've mentioned you'd liked to have seen a little more informal think tank type activities.

Manaker: You know, if I were thinking in terms of the field as it developed and what was going on, do you know that perhaps we started off with a little too much. You know, I think, looking at that in retrospect, you can have too much funding; too much, because then there is less regard for the quality and too much regard for quantity. I don't know if I make myself really as clear--

Baker: I don't know that I agree with you. I understand what you're saying.

Manaker: No, no, no. You know, what I'm talking about is whether--

Baker: It doesn't have to be.

Manaker: No, it doesn't have to be. But, you see, there are just so many investigators.

Baker: And I thought we worked hard to avoid that.

Manaker: There are just so many people out there, just so many out there that can do the work, so many labs. There are so many major centers, there are so many university laboratories and so on, here, there and everywhere. And if you are a little strained about being able to fund all of them, then maybe some guys don't get the money but, on the other hand, the guys that get it probably are the "bestest" choice that you could make at the particular time. You don't have enough to be that generous to yourself--not to them, but to yourself--to say, "Well, I would like to fund this and this, but no, I have to make a choice and it's got to be here for these reasons." In other words, maybe the decisions would be harder and colder and provide more input for the expenditure than it would be if you have a little bit extra to where it's too easy to, let's say, spread it around. I don't know. I wonder about that.

Baker: Well, you have to hit a balance between that problem and how do you expend the amount of effort that should be brought to bear if you think the problem is that important. Your plans should always be ahead of your funding.

Manaker: Yes. That's right. Well, there you are.

Baker: So it's timing, partly, too. So it's a complex subject.

Manaker: Yes. It is a complex subject. Yes.

Baker: I always tried to look at quality. I felt that NIH, in those days, emphasized quality enough that what you're bringing up wasn't--

Manaker: Well, I don't think we had any extra left over there.

Baker: No. Because my answer to that was your planning should always be ahead of your resources. And then what resources are you going to need? And money is only one of them.

Manaker: Yes. I think the limitation is really on what's out there, not what you've got in your pocket. That's right. You're right.

Baker: Number Nine, you've already said, yes, you feel it has.

Manaker: Oh, yes. I don't really know that it could have gone to the extent that it did now without this.

Baker: The amusing thing about the National Cancer Act of 1971 is that most of us who were there before that saw developments as a direct continuation of what was going on before.

Manaker: That's right. Yes.

Baker: But the way it's described now by those who didn't live in the older periods is that all of a sudden it was different. And I think most of us old-timers just see it as just a continuation.

Manaker: Just a continuation. Yes.

Baker: And with respect to some of the results in man, the research findings that led to them, were way back at least 10 years before.

Manaker: Can you imagine suddenly running up against something like AIDS without the background that was derived from all of these studies that went on in the Program? You know, a whole different kind of agent?

Baker: Of course, we're not doing too well even with the knowledge.

Manaker: Well, I mean, that isn't the point. But the understanding is there. What this agent does, the way it's expected to behave, why it's hitting this particular kind of cell. Yes.

Baker: The tenth question is a little different direction. It's not talking about the program, per se, but the public's perception of science and biomedical activities. Do you think the understanding, on one hand, and the sympathy for, on the other, are different now than they were when we were at NCI, or better or worse?

Manaker: Well, I think that probably the whole thing might have been at a more emotional level back about that time. But, no. I think people were also a lot more worried then. Do you remember all the fuss and bother about having anything going on in my neighborhood, or so on, the idea of having a building like the one that we have for containment out there near any kind of an area like Bethesda so close and the worry that people would have, all the fuss and bother, about how far you might expect to have dissemination of an aerosol, and all this fuss that went on, and the building of the Ft. Detrick kind of big containment facilities and so on which, in a sense, sort of evaporated, didn't it?

Baker: Well, now they're focusing on the incinerator at NIH.

Manaker: They're focusing on--yes--a different kind of risk, right, which is a joke too.

Baker: But you don't feel there is much difference in the public's support of science?

Manaker: Oh, I think people are much more prone to support the science. I don't think that you would have quite the same response--

Baker: Are you aware of the creation of the Office of Alternative Medicine at NIH? Do you know what that is?

Manaker: No.

Baker: Well, it's not quite astrology, but it's almost that bad.

Manaker: Oh, you mean almost like the acupuncture approach? That sort of a thing?

Baker: That's one of them. It's a sub-program.

Manaker: Yes. I've heard a little bit about it, but I don't know too much about that. But it's the idea of using the Chinese kind of herbs, things, and so on.

Baker: It's an idea of setting up funding for these "way out" things such as acupuncture and not quite astrology, but almost. So, I'm very worried about this, but--

Manaker: I am too. Really. I think that it would be all right as a small probe, but I sure in heck don't think that it's worth any kind of really going hog-wild over.

Baker: I understand they made $15 million dollars worth of grants this last year.

Manaker: No kidding? Oh, my gracious sakes.

Baker: This is all because a Congressman was pressuring NIH to set this up.

Manaker: Well, that's how it goes, doesn't it?

Baker: Why? Because his wife had a chiropractor that helped her, or no, homeopathy. I'm sorry. Homeopathy.

Manaker: Oh, my gracious. Well--

Baker: So, that worries me.

Manaker: It worries me too, really it does. But this stuff they get--

Baker: Because this, to me, is a slipping back of knowledge or even civilization.

Manaker: Because if it's worth a look, well how much of a look? And how much really does it take? I don't think it takes $30 million dollars, for goodness sakes, to get in there, to have a kind of well controlled study, or to look into that thing.

Baker: Well, I kept thinking about it. If you could have a well controlled trial on acupuncture, it might be well worthwhile. But, I looked into this and there is no agreement among those who do acupuncture on what is <u>the</u> way to do it. So, if you tried one trial and no difference was found between the controls and the experimental group, then they'll say, "Oh, well, he didn't do the acupuncture right, so give us some money and we'll show you how to do it." And that will go on and on and on.

Manaker: Right. Too much of a big, deep barrel.

Baker: Any additional comments you'd like to make?

Manaker: No. I think that we've discussed it-- Well, you've listened enough. I'd hate to have to go over this thing with you, you know, because it's such a rambling thing.

Baker: Well, we're probably not going to do much detail, but it's to get a flavor and a few anecdotes here and there. And so I appreciate very much your time and effort, and it's good to see you again.

Manaker: Yes. Well, do you think that I provided anything that's going to be useful?

Baker: Oh, certainly. Certainly.

Manaker: And do you think that your efforts along this line on the Program will really be worth all the work that you'll have to do?

Baker: Who ever knows? But I think it needs doing anyway.

Manaker: Yes. It would be nice to have it done.

Baker: You were making a general comment?

Manaker: Well, without the Virus Program, certainly I don't think that we would be, in general, looking at the kind of scientific activities that are going on in this field right now and that we would ever have been able to be at the position that we occupy or the position that we do now without having all of that background work that went on over the years--the investigations and such, the probing, even the false leads and so on that might have developed--had the program not existed.

The interest of the general scientific public in this kind of an activity in these areas of investigation certainly would not have been aroused to the extent that it was now, and certainly there would not have been the directed effort that you have not just here, but abroad, to go into these areas of investigation dealing with these viruses such as AIDS which belong to a group of agents, the retroviruses, that we now know so well would have been anticipated. I think that whatever it was, it was cheap. The money for the information we got was cheap.

Baker: Do you think the planning that Rauscher and Carrese and I did together had much influence on this?

Manaker: Well, I don't see how the thing could have started without the planning and, in fact, the way it was laid out at the beginning indicated the way one had to go. I don't think that there are any shortcuts beyond the way that thing was laid on out to get in there and to get a workable something in hand, a workable approach, to a problem in this particular area without that kind of a plan to have begun the overall investigation.

Baker: Were you involved when Zinder and his committee reviewed the program?

Manaker: Not really. No. No.

Baker: Did you read that report?

Manaker: I didn't read it.

Baker: Well, I won't ask you to comment on it then. Okay. Thanks a lot.

Dr. Baker adds:

NOTE: I might mention that Bob Manaker was a pilot during World War II, first with the Army Air Corps, and then, when the U.S. Air Force was created, he moved over to that. He flew planes that picked up personnel and ferried them to different places in a rather large airplane. He also has a couple of interesting hobbies. His oil paintings are excellent, and he plays the organ.