

Oral History Interview: Dr. Charles Boone, Virus Cancer Program
Interviewer: Dr. Carl G. Baker, former Director of the National Cancer Institute
April 19, 1995

Baker: Chuck, would you start us off on this interview by telling us a little bit about your background, where you went to school and so on?

Boone: Okay. I went to college at the University of Texas, medical school at the University of California, San Francisco, internship, L.A. County, immediately after internship 3 years as a family practitioner in Los Angeles. Then I went for a year as a graduate student of Linus Pauling at CalTech, and took all of the graduate courses required for that. And it happened to be in '53, at the very time when the Watson-Crick model was announced, when sickle cell hemoglobin--Harvey Itano--was at CalTech, so it was a thrilling time and actually made me realize I wanted to be a scientist more than I wanted to be anything else. So, that's why I went to CalTech. But after a year this course work was so foreign, because I had a degree in medicine and an internship, that I decided to go into pathology, which I did at UCLA. So, for 4 more years I did residency training in pathology, anatomic and clinical. Then, after taking the Boards, still having the research bug, I went ahead at UCLA, in the Department of Biochemistry, and did four more years yet in biochemistry and wound up with a Ph.D. in biochem.

Baker: Who was your mentor there?

Boone: Emil Smith, who is still there, was the Departmental Head, and no one would remember the name of the department member who was my immediate mentor, but Emil Smith was working on the structure of proteins and my particular thesis--

Baker: Yes. I know Emil Smith.

Boone: Okay. My thesis at that time was to culture tumor cells, which was a big deal in those days, and to compare normal and neoplastic cells in culture by biochemical methods, which I did for my thesis. And out of that grew, of course, awareness that Harry Eagle had similar ideas and skills, and so I did a postdoc with Harry Eagle in the Bronx. Now, we're at 1965. I'm going to skip ahead and give you my whole background quickly nevertheless. I came to NIH, thanks to Bob Stevenson. I developed a cell biology lab. For a total of about 15 years I had a nice lab in Building 37. In 1980, I left for a year of retraining at the Mayo Clinic in pathology, following which I went to Saudi Arabia for 3 years as a pathologist, a practicing pathologist, in a big hospital in a town called Taif. I had a good time. I came back with lots of money and wound up, after a year or two of wondering what the hell to do, with the Chemoprevention Program here at NCI in its very beginnings. I stayed with that for a while. Then I decided to retire early, which I did, and I did a couple of years of residency training in family medicine--this is official residency training--at the University of Maryland for the first year and the University of California at Irvine for the second year. This is now '86 to '88. Now I was trained up in family medicine and my conception was to take the money I made in Arabia and retire in Arizona.

I bought a condo there and I was going to affiliate with the University of Arizona, be a *Marcus Welby*, and fiddle around with basic research. That was the basic idea. After my training in family medicine in '86 to '88, I wound up going back to Saudi Arabia as a family practitioner for another year, and that really added to the bank account. So I was able to come back and, at that time, using the few years in the Chemoprevention Program as the background, I came back to this area specifically for one year only to write a review of chemoprevention, which I did. Then I was going to go to Tucson and spend the rest of my life happily retired. But I never left, coming here for that one year, and I've been here ever since. So, that tells that part of the story. I guess that covers most of my background.

Baker: That's quite an interesting variety and mixture.

Boone: Yes.

Baker: Were you close enough to Pauling to see his reaction when the Watson-Crick announcement of the structure of DNA was made?

Boone: I was there at the time that Linus Pauling constructed his erroneous model of DNA. I was there. I saw Watson interacting with Pauling. I was there when the actual correct model was produced. And Pauling was a vivacious, hyperactive, not quite feet on the Earth individual, who was a brilliant statistical mechanics mathematician. Few people realized that. His power was in his mathematical knowledge. He trained with major mathematicians including Schrödinger himself, so he knew the Schrödinger equation from the master, and he used it.

Baker: Fine. I think that gives us a pretty good background, so we can turn to the questions next. And the first one, of course, is getting your impressions of who comes to mind, and what are the five, or more, most important scientific results highly significant to the virus cancer field during the period 1950 to 1980, and who were the key scientists?

Boone: Well, 1950 is the end of the era of Payton Rous's discovery that chicken sarcomas were induced by a virus and that also a virus does indeed cause cancer in rabbits (with the myxomatosis virus). Joe Beard's and Ray Bryan's extensive work with the Rous sarcoma virus had also reached a mature stage.

Baker: I think what Bryan did was quantitate it, to show a dose relationship, which is a strange thing in a sense, if you think of a virus as an infectious agent.

Boone: Yes. It is. So, this was the first announcement. And then, incidentally, I remember Renato Dulbecco--I turned out to be his Project Officer later--had made some profound, at that time, discoveries that he could actually produce cancer in tissue culture by adding a virus to a monolayer. And this was just when monolayers were coming out. I was a resident in pathology at Harbor General Hospital in Los Angeles, and I got a scientific journal showing a glass capillary tube with outgrowth of fibroblasts produced from a single cell for the first time. The work was done in Wilton Earle's laboratory by a woman named Katherine Sanford.

Baker: I went to Katherine Sanford about 3 months ago. I've still kept up contacts with her and we're collegial and I have the data for a paper that we've actually cooperated on. And we were chatting about the old days and she said, "You know, I'm going to be 80 years old soon, and I think it's truly about time for me to retire." You know, the proudest, and best, and most flinty administrators and branch chiefs in the world have tried to get rid of her and every one of them have stubbed their noses hard. So she stands there resolute that she's going to retire when she feels like it, and it's going to be soon, another six months. So I said, "My God, Katherine, let's have a grand bash, because this really would be an event. Let's call in all the old people?" So we got a copy of the TCA, the Tissue Culture Association, journal membership and looked over who we'd invite, and it turns out that most of the people that were active in the important era are now gone and there aren't that many people left who would come for a farewell bash to Katherine Sanford. But for Robert Stevenson, of course, it would be wonderful.

Baker: One of the worst things about growing old.

Boone: Yes. I agree. But we're all going together.

Baker: I just remembered that you wanted to mention something about your influences from the literature in your early years, very early years.

Boone: Yes. Okay. I started out-- The thing that made me what I am today was reading Sinclair Lewis' *Arrowsmith*. Then I read *The Citadel*. Then I saw the movie with Robert Donat, and that absolutely sunk it. And for flavor, which I doted on, was Lew Ayres and Lionel Barrymore in *Dr. Kildare*. Now, it turns out I actually repeated that in real life by being an intern at L.A. County and where I went to the same old greasy spoon across the street. I did as much unconsciously as I could to imitate Lew Ayres at that time, and anyway, out of that *Arrowsmith* experience, that's why I kept trying to get back in the lab. That's why, after having a board certification in pathology, I still wanted to be a researcher, and I went and got a Ph.D. in biochem. That was imitating Martin Arrowsmith, and when I went to get the Ph.D. I was supported by a training grant from NIH, and there was a man named Shannon who was the Sun--he was the God Ra--and his radiance illuminated and stimulated and was the blood and breadth of the life of very basic research. And that's all there was: wonderful Martin Arrowsmith basic research.

Baker: Well, fine. I wanted to get that in. Let's go back to the first question. What key scientific findings do you think led to the shift from no interest in viruses in cancer to the beginning of interest which has blossomed so much since then?

Boone: Peyton Rous played around with chicken tumors and showed that they were caused by a virus.

Baker: But, you see, nobody was too impressed with that.

Boone: Well, but he published some pretty good papers in *The Journal of Experimental Medicine*.

Baker: Oh, yes. They finally got recognized with a Nobel Prize. But, at that time, there were only about 3 or 4 people that were doing any work in

viruses and cancer. So, what happened to change it?

Boone: Well, Renato Dulbecco discovered you can make cancer in a test tube. That was a big deal. That's what I remember. Viruses. Ray Bryan. These were the only findings. Of course then, here comes Huebner with his hypothesis, and that's a little bit later.

Baker: That was a good bit later.

Boone: That's all I remember.

Baker: Well, I'll give you a hint. It seems to me that Ludwik Gross's showing that you could induce leukemia with cell-free extracts--

Boone: Oh, the milk factor?

Baker: No. The milk factor was Bittner.

Boone: Okay. But Ludwik Gross worked with--

Baker: Nobody believed Gross for a couple of years, and then Sarah Stewart, of course, with the polyomavirus.

Boone: Oh, yes, yes, yes.

Baker: So, once people confirmed their work, you had a whole change, and people began to get interested in viruses in cancer, including *in vitro*.

Boone: Yes. But didn't Gross work a great deal with the transmission of mammary, mammary tumor--

Baker: It was mostly leukemia. And then he got a polyoma too which--

Boone: Isn't he the guy that showed-- Wasn't it Gross who showed--

Baker: Bittner is the one that had the milk factor.

Boone: Oh, I see.

Baker: And he and Bryan--Bryan did a lot of the genetics on that also with Andervont.

Boone: Okay. When Robert Stevenson--

Baker: But that still was aberrant.

Boone: This is going to be directly in response to your question. When Robert Stevenson came to Harry Eagle's lab to say hi and coaxed me down to NCI, I finally accepted and we were off and running, and the very first thing that happened within two weeks of my recruitment was that I went to a meeting in Philadelphia where all of the important personages related to viruses and cancer were assembled to talk. I'm blocking on the name of the guy at the Wistar Institute--he's still there--Kowproski--but Kowproski was there, Sabin, Lennette, Melnick. Alexander Rich was a big speaker. Sarah Stewart was there. What's her name, Mary--the one who worked with the antibody developed from injecting bone marrow and then absorbing it like hell but not quite enough for it to work well. so she always had-- Mary--I've forgotten her name--Fink. So, she was there. I remember they had excellent brandy and cigars for dessert.

Baker: Was this the birdseed guy that sponsored this meeting?

Boone: I think it was at Wistar.

Baker: Do you remember that there was a series of meetings sponsored by the man who owned the Hartz Mountain company that sold birdseed? I can't think of his name at the moment.

Boone: Birdseed? I don't think so. I think this was put on at Wistar, but I'm not sure. But anyway, Robert Stevenson thought it was something I should see and, by God, it was. It was a hell of a thing. A big, quick

introduction to viruses and cancer. We've talked about the people now and their findings. Of course, polyomavirus was a big deal, and Sarah Stewart was in there. So they tracked down the trail of the potential for a virus that caused cancer, and it was a very, very, logical, obvious thing. So those are the key scientists involved at that time.

Baker: Well, that covers the main highlights, which is all I'm after here. So, the next question shifts from the scientists to the administrative or management decisions that affected this area and who made them as you remember?

Boone: All right. 1969, as I remember--this is all I remember now--I came here in '65, and '69 was the "Moonshot Memo" to Congress by Robert Huebner. Now, there's a guy named Endicott. This is when I was a little ragged in my life. This is true. Anyway, Kenneth Endicott got intrigued with the virus cancer idea--I know that--and I know that Huebner was over in NIAID and I know that Carl Baker was--it's a little later now, this was about '68--Carl Baker was actually working with Lou Carrese and I've forgotten the name of the--

Baker: The Convergence Technique. And it was 1963 and 1964.

Boone: The Convergence Technique. Yes. PERT.

Baker: Well, we didn't like to call it PERT, because it had differences.

Boone: And McNamara was the "God of Careful Analysis of Programmed Research," and it filtered down conceivably. Somebody should talk to Jack Gruber because he knows about a very important helicopter ride with Nixon and Rauscher going to Frederick, where Nixon decided to change it into a cancer center. But that's another story. But these are important personages.

Baker: This is not accurate. Just before President Nixon announced making Ft. Dietrick a cancer center, Zubrod, Rauscher, and I briefed the President on the current status of cancer research. There was no such helicopter ride at that time.

Boone: Okay, so now management. Carl Baker monitored, that is he godfathered, he tried to keep under control, some bucking broncos named, in particular, Melnick. Now, there is a guy, Ray Guilden-- Stevenson took me over to the ground where they were constructing a laboratory that was going to be called Flow Labs, and Robert was busy talking with Ray Guilden, who was going to be Huebner's super-manager person. And we met Masakazu Hatanaka, who was in my lab during the Program, who was a Virus Cancer person trained in France at the Pasteur Institute. I saw Ray just recently. He is the way he's always been. He's pragmatic, smiling, engaging, smart. Bob, I think, used to like him. I sure did. Now, what Ray Guilden said is that he worked with Huebner for many years and was his whipping boy and eager lieutenant, super-lieutenant. He said, "You know, Huebner used to think that he was Alexander the Great and, you know, he was." So, Alexander the Great is this guy who really thought he was God's gift to cancer research over there in NIAID. And here's Carl Baker trying to keep a lid on this mountain that was forming. Anyway, there's something about a National Cancer Act.

Baker: I object to being characterized that way because I thought I stimulated

more than I kept a lid on.

Boone: Well, you were there, trying to keep it together, I thought. That was my impression.

Baker: Keep it together, but not keep a lid on it.

Boone: No, no. Okay. I didn't mean that.

Baker: Look at the budget, if you think that.

Boone: That's right. You were trying to keep things integrated in some kind of rational structure.

Baker: Integrated relationship among the parts. Yes.

Boone: That's right. That's absolutely right, and that's how I remember you.

Baker: Huebner was an interesting one to have in that situation.

Boone: Huebner was not of this Earth. You were a rational human being, trying to keep things within reasonable structure. That's all. That's what I think. You tried to put structure onto Huebner's vast mentality, at least part, and that includes his pals Sabin, Lynette, Melnick, Maurice Green.

Baker: I never thought of myself as putting a lid on any of them.

Boone: What you tried to do was to keep it coordinated so it was a choreographed operation instead of a one-man show going wherever he felt like.

Baker: Yes. Put it all together.

Boone: Yes. And that's the way it came off. So now, boy, were those the days. This was '69 now.

Baker: You then came after the Special Virus Leukemia Program had already been founded?

Boone: No, no. I came during the Special Virus Leukemia Program.

Baker: Well, but the \$10 million had already been appropriated from the Congress.

Boone: The "Moonshot Memo," the \$10 million--

Baker: You see, the "Moonshot Memo" is much later than the original request for Congress for a Special Virus Leukemia Program. That was in '64.

Boone: Okay. That's where I came in.

Baker: The "Moonshot Memo" was '69 or so.

Boone: That's right. Sorry about that.

Baker: So a lot happened in those years.

Boone: I came in Special Virus Leukemia and, as Bob Stevenson well knows, I enjoyed the concept and the job and I've always enjoyed it, which is the idea of organizing and managing a Human Tumor Procurement Program, which I think was very rational. And I did that, and we had a good time.

Baker: So, that brings us to the third question of what do you consider to be your main activities and the effects of your participation during this period?

Boone: I've already started on that. Have I talked about the major players and ideas and things? The Special Virus Leukemia Program, Ray Bryan was in there. Carl Baker. and Endicott. Endicott and Baker were trying to put rationality and administrative reality to what promised to be an explosive harangue and mismanaged who-knows-what, depending on what some of the investigators wanted to do. These were basic science oriented people who would throw up if they thought about programmed or applied--they called it, that was the buzzword--"applied" research.

Now, my contribution was to manage a Human Tumor Procurement Program for Robert Stevenson in Robert Stevenson's Branch, which I did, and things were going very well, and Bob was content, and I was content. Now, something happened and Robert Stevenson left NCI. Yes, that's right. About the time of the "Moonshot Memo," there was a change in the guard. And that's when a special act of Congress in '69 made a separate institution, sort of--Act--out of what used to be part of NIH.

Baker: I'm sorry. That was late '71. The Cancer Act did that.

Boone: That's the Cancer Act?

Baker: That was later.

Boone: Something was happening-- Oh, that's right. You were there from '68 to '71?

Baker: I was Director '69 to '72.

Boone: '72? Okay.

Baker: But the new Cancer Act started at the end of 1971. The President signed the Bill the day after Christmas, '71.

Boone: Huebner was active. That was it. Huebner teamed up with George Todaro. That's right, Huebner and George Todaro.

Baker: They had already written their paper on oncogenes.

Boone: They invented the word "oncogenes."

Baker: That was before your "Moonshot Memo" to Congress. The Huebner-Todaro paper was in a scientific journal.

Boone: Yes. I was actually in the Wiscon Building about ready to go over to Molloy Labs to have my Cell Biology Section, my heart says to good old Bob, "Thanks a lot, Robert." I was really grateful for that. And here is this guy who came to me. We were going over stacks of 2-year wonders, looking for who we were going to recruit. And so I was sitting there, minding my own business, and in came this person named George Todaro. Now, during my internship and my postdoc with Harry Eagle, George Todaro was already a well established person, a trainee of Howard Green. Green developed the 3T lines, 3T6 and 3T3 and trained George Todaro. And so George developed his own lab at Moloy and became very chummy with Huebner and, out of that, somewhere, Bob Huebner got switched to NCI, I believe, for Rauscher and I think Carl Baker had something to do with that, as a matter of fact. I'll bet you did.

Baker: Yes, very much so.

Boone: I'll bet you did. I'll bet they decided they also wanted a name personality who was young and could be controlled?

Baker: Well, not "controlled." I don't like that terminology. I considered Bob Stevenson one of my best program leaders because he had a grasp of the science and he was a good manager both, and that's what you need.

Boone: Yes. But Rauscher was better because he had a name that was marketable, he was young, and yet he was naive enough so he wouldn't try to take off like Huebner. But I'll leave that for you and Bob to deal with.

Baker: But Rauscher knew the field and was fairly broad, at least in biology of cancer, and he had a good leadership personality.

Boone: They needed somebody to hold the fort until Huebner came over too, by

the way, something about that. I've forgotten what it was. But there was a period when the branch was vacant, and I think that's--I may recall wrongly--that's when Rauscher--

Baker: When Stevenson left the Institute?

Boone: Stevenson left. That's right.

Baker: Yes. He went with Union Carbide.

Boone: Yes. Now I remember. Stevenson will easily remember the name of the pathologist who was the Director of Etiology who now is in Colorado working for Ralston Purina. He was trained at Oak Ridge. He knew all about respiratory--big time, respiratory aerosol carcinogenesis. That was his big thing. I can't remember his name. But he preceded you, I believe, or followed you, as Director of Etiology.

Baker: Oh, you're talking about Paul Kotin.

Boone: Paul Kotin. Ralston Purina.

Baker: Well, I guess he went with them first, but he really went with the asbestos people.

Boone: He was a big-time asbestos person.

Baker: He got caught in the midst of the asbestos lawsuit.

Boone: Oh, boy. But he was right in there. But he worked with Oak Ridge and so on. I was interacting with him a lot because of my training in path. And I've seen him since. So, to get back on track, where are we? We are trying to identify important personages--and Carl Baker was one--who was administrating all of these broncos. Huebner, in particular, was a great big situation that you tried to integrate into a larger program, which you did, I think.

Baker: Yes. I think we did.

Boone: Okay. Then the "Moonshot Memo," and taking off from there. That's the best I can do.

Baker: Well, that takes us down to question five, and that turns to looking at key committee members and individual consultants. Now, you've already listed the--

Boone: Now, Bob used to call them the Schlemiel Committee.

Baker: I never heard that before.

Boone: He'll remember, and smile, I hope.

Baker: And that stands for Sabin--

Boone: Lennette, Huebner, Melnick. Those four individuals.

Baker: They were certainly very helpful advisors, both on committees and as individuals.

Boone: Oh, I think they were outstanding, and we were lucky to have those people at that time.

Baker: There was another man who chaired one of the committees earlier, whom I don't know if you ever came in contact with, Chuck Evans from the University of Washington Microbiology Department. He was one of the best chairmen we ever had for keeping things not only on an even keel, but right on target.

Boone: Wait a minute. Let me tell you about Robert Stevenson. Let me tell you about him. I actually can say more about him probably than anybody I know. Do you know that? I'm going to do it now. Robert E. Stevenson,

first of all, his command of the English language is the best I have ever seen in any administrative mentality. His rhetoric and diction, his choice of words and phrases, were so good that when he left he threw out all of his old correspondence and I still have some of that correspondence as a model for how to write a memo. Second to none. He could really ring the rhetoric. Okay? That's number one.

Number two. Robert Stevenson had a certain managerial persona. You know that.

Baker: That's what I'm saying. He not only understood the science, but he was a good manager.

Boone: He was more than that. He knew science quite well. That's right. But I'll tell you about this persona. To me, to this day, he would have made a tremendous manager-administrator anywhere and the reason why; you could never get to him. You could get close, but that's as far as you got. You never could reach out and touch him. Okay? And that's a tremendous advantage when you're an administrator because once you're palsie-walsie you've already biased somebody.

Baker: Or you have to be palsie-walsie with every one of them.

Boone: That's what Robert was. Robert was smiling everywhere but with no one, to my knowledge, did he ever truly confide what he was really thinking. Okay? And so, for that reason, he was a little fearsome, I think, to everybody.

Baker: That's interesting. I hadn't thought of it that way.

Boone: Well, he was to me too because he was my boss, and I was young in those days. Maybe I wouldn't think he was fearsome now. But I've always liked him a lot, and he knows that, and I think he's a little mystified. "Why in the hell does Chuck like me?" "I like you because you were a thinking, rational, calculating, competent human being." That's why I like him.

Baker: Nicely put.

Boone: There you have it. Robert, now, one other thing about him. A lot of people didn't like him because he didn't have a strong power base. Nobody gave him a power base, by the way. People were too enamored of names like Rauscher and Moloney.

Baker: I put Stevenson at the same level.

Boone: No. Stevenson--

Baker: I personally put him at the same level.

Boone: Well, he didn't discover a virus. If he had discovered a virus--

Baker: But he still made great contributions. We're not here to praise him or bury him either.

Boone: What I'd like to just say now, being practical, I'm saying, at Airlie House, when he got up to speak, he had things to say and he was among the most rational managers I've ever listened to. Okay, enough of him for now. Now what?

Baker: Are you aware of any lay individuals--

Boone: Benno Schmidt.

Baker: --or political people who had influence here?

Boone: Benno Schmidt. There were two others, I've forgotten who they were,

but Benno Schmidt was the leader of a "triumvirate," we used to call it, that would advise Nixon in particular. And whatever that man thought is what happened. That much I know. It's funny. I knew somebody who knew him quite well. It was a woman. But that's another story.

Baker: Well, he was certainly a very competent person. The other original members of the President's Panel were R. Lee Clark and Bob Good.

Boone: Yes.

Baker: I think it's fair to say that when Benno Schmidt was head of the President's Panel he actually ran the NCI program.

Boone: Right. He did.

Baker: Rauscher was the Director, but as near as I could tell, Benno Schmidt was the man that was running things.

Boone: Yes, indeed. Yes, indeed.

Baker: And, of course, Mary Lasker was a very influential person in all of this.

Boone: Yes. Interesting, it's very, very true. I've watched her over the years. I watched her grow old and finally pass away. Always a valuable person to our culture.

Baker: She certainly contributed. She could be worrisome sometimes, but she made great contributions.

Boone: Right.

Baker: Sidney Farber--

Boone: Oh, Sidney Farber.

Baker: --as a scientist-politician played key roles, I think.

Boone: The consummate politician, methotrexate was his big thing. That's what made him. Sidney Farber. However, don't forget Emmanuel Farber, not to be sneezed at.

Baker: Well, I think he was much more influential in the scientific side than he was in the management side.

Boone: Right.

Baker: In fact, he never accepted the planned programming particularly.

Boone: Oh, is that so? Well, Harry Eagle never did either.

Baker: Well, I got Harry to admit at a meeting one time though that some of it was all right, particularly on resources, and then so I said, "Well, Harry, all we're arguing about is the relative amounts then, if you accept that."

Boone: Well, Harry was adamant-- I spent a year listening to him.

Baker: But I had him as one of the advisors because I didn't want to just have everybody that was gung-ho for it. I wanted criticism too.

Boone: Well, the prevailing view during the Shannon era and the Arrowsmith mentality objected vehemently to targeted or programmed research and I'm telling you, and I'll tell Robert, I clearly remember people who really acted as though they preferred confusion and beating the bushes of basic data, rather than anyone taking a step in the direction of integration of research efforts, because that was applied, and being applied was a terrible, terrible thing in those days. Very interesting. And these Department of Defense hotshot contractor people thought they were running things in certain areas. You know about that?

Baker: Yes.

Boone: We have a lot of trouble getting anything done by contracts now, but

Huebner had a guy named Lou and all Huebner had to say was, "Put this guy on," or "Give this guy so much money," and it happened. And so, to this day, I'm one of the few people who knows what can be done with a Contract Program if you have enough agreement.

Baker: I might ask a couple of questions about the review. Another point here is that many people, particularly in academia, thought that the contract proposals got inferior reviews compared with grant applications.

Boone: In my opinion it was all the same. The important thing, however, if you have a tight-knit bunch of intelligent specialists, all of whom know what the hell should be done and who should get it, it's very difficult to be objective. The ultimate in objectivity is complete mediocrity.

Baker: Therefore, objectivity is not necessarily the objective?

Boone: No, subjective passion to move and make something happen that they believe in.

Baker: Do you think things are different now in that regard?

Boone: I think they're just the same as they always have been and always will be.

Baker: You don't think that there is more politics now than ever before?

Boone: I accept it now because I'm old.

Baker: Yes. But is it any different? Is there more--

Boone: It's no different.

Baker: Do you think there was as much politics then as now?

Boone:J ust exactly almost the same perhaps, except we didn't have the colorful figures. I don't think anybody put somebody on the wall, the way I have Huebner's picture now. I thought that that experience could be revisited.

Baker: That was part of the idea behind the planning, so you could show people what the money was going to go for.

Boone: Yes. That's true.

Baker: And remembering always that plans should be changed at least every year and a half. Keep them updated.

Boone: Well, there were a lot of people who demanded to know what the hell is happening with the money. They wanted accountability. And that's one of the things you gave them.

Baker: Well, there's nothing wrong with that either.

Boone: No. That's what I'm saying. You gave them that.

Baker: The public ought to expect that.

Boone: Yes.

Baker: But I was very careful not to over-promise though. I never slipped, like DeVita did, and said, "We'll have such-and-such done by the year 2000," or something.

Boone: No, no. I mean this. I'm not being complimentary. I thought that everyone was content under your aegis. That's important to say. You were a person--

Baker: As long as they weren't lackadaisical, that's fine.

Boone: Well, you were a person that tried to rationalize it in a way that could be explained to Congress so that the money would continue to flow.

Baker: The plans were useful and the Bureau of the Budget staff thought it was about time somebody from NIH told them what they were going to do with the money.

Boone: That's great. That was a tremendously good thing.

Baker: Okay. Let's turn to the area you were most directly involved in, on the significance of the quality controlled--and I use that advisedly--resources.

Boone: The significance? Okay. Well, let's get into that a little bit.

Baker: And then I want you to paint the picture of how it was, say, in 1955 compared to--

Boone: Well, they were nowhere. No, no. Wait a minute. Hold it. There were a whole bunch of labs, all of them supported by basic money. There was no coordination between reagents or materials. Everyone had his own little thimble-full of highly purified characterized stuff which he very stingily would give to somebody else as long as he was a collaborator and his name was on the paper. That's the way it was. That's basic research.

Baker: I once told virologists from the polio game--and this is when I was with Smadel--that they did a very good thing. They were insisting on quality, and so they would always exchange samples with each other when they isolated a virus but, by the time they'd exchanged all their samples, they didn't have any left to work with, and we had to get larger quantities. If we did it on contract we could get quantities needed, and, if it's not good enough to meet your tests you don't have to use it.

Boone: You remember Norman Anderson promised to deliver kilograms of virus--nucleic acid--viruses, packed viruses, in his ultracentrifuge. That was a tremendous step forward because it gave the unification--standardization--of reagents so that things were available that would be reliably the same today as tomorrow.

Baker: Yes. This was crucial.

Boone: A tremendous thing. Now I think that should be strongly emphasized.

Baker: And I think that a lot of the virologists did that but, as I say, they didn't really have enough to do much with after they used up all their supply.

Boone: Right. And Robert Stevenson gets credit for that concept. The whole thing. Robert's ideas didn't stay with just viruses. They went on to cells and then tissues. And today, even today, that could benefit people. Some of his ideas, particularly when you get up into tissues, where I lived, died when Robert left and they shouldn't have.

Baker: Okay. Where are we? Okay, resources and reagents--

Baker: We know today that a lot of this stuff is commercially available so, do you think the Viruses Cancer Program, by developing these large amounts of quality controlled resources, has affected then the commercial picture of availability? That's a loaded question, obviously.

Boone: Yes, it is. I think, as a matter of fact, there was no commercial company, unless it was given a big contract from NCI, that could have done the same thing. And you needed standardization. There is no way to get standardization among competing small companies

Baker: It's pretty hard with grants too.

Boone: There's no way. I mean, the thing was justified from the word go, so there is no problem with that. They could scream all they want, but they couldn't ever come up with something as good.

Baker: You probably were not aware of the relative amounts of funding in Virus

Cancer grants compared with Virus Cancer contracts?

Boone: No. But I know there was tremendous complaint by these austere-- I used to characterize them as being patricians with purple borders to their robes. And they would never be tainted with the concept of trying to integrate their ideas into something that had a practical goal. The minute you start to get practical that was applied, and they were basic. They had to remain obscure and confused. And I stand by those words--obscure and confused. That's what I'll say.

Baker: Well, we've come to the difficult question. If you could have changed anything, going back, in the Viruses Cancer area, what would you have suggested?

Boone: In the Virus Cancer area, if I could have changed anything--

Baker: Particularly in the Program, but even outside.

Boone: Change it? Well, my bias is based on my training, and I was trained in statistical mechanics at CalTech by Linus Pauling, and all the advanced math. I was trained as a pathologist so I can look at all the tissues and see what cancer really is and in clinical areas. I've watched people give lectures where every point on the survival curve is another agonized parent whose children watched tearfully as this big, bulky, bleeding mass kills them. And, out of all of that, I'm convinced, and was at that time, that yes, chemicals cause cancer, yes viruses, yes physical x-irradiation, because, as you know--this is your favorite theme too--disorder is the key, and that wasn't understood by the virologists. Now wait a minute. Let me digress on this a little bit. Sir McFarlane-Burnett, Stevenson used to say, about that time, "Those who think that cancer is like an infectious disease and is caused by a single entity, who think deterministically and want to abide by Koch's postulates, those people who think that cancer is like an infectious disease are wrong. Those who think that it's like a virus deficiency, a one-on-one relationship between cause and effect, thinking deterministically, is wrong. It's not an infectious disease; it is a stochastic process that has a multifactorial cause." And he was right. And so most of the virologists were thinking deterministically and felt it was like an infectious disease; that they could find an infectious agent that causes cancer, they would give it a vaccine and cure it. That was wrong. And I swear to God, I swear to God, I knew it at the time. I always knew it. There was no one around for me to talk to. There were no pathologists. No one thought anything but virology and I was swamped by Ph.D. virologists until I was smothered to death.

Baker: Well, when I came to head the Etiology, on chemical carcinogenesis in particular, I wrestled with this difficult problem of cause and effect. It's a very difficult subject.

Boone: Yes it is.

Baker: And I concluded as you're suggesting, that most things are not simply A causes B; it's A, B, C, D, E, F, in varying proportions and strengths, at different times, combine sometimes to produce effects X, Y, Z, maybe.

Boone: Good. And when you take one of those factors and enhance it, you can make it a single cause. The best idea is to--

Baker: It's how you define it, in part.

Boone: Well, you and I used to talk about this in those days and, by the way, you thought the same way I did. You thought it was a disorder. You know, you put a gun to the head and pull the trigger, that's cause and effect, but if you take a shotgun and shoot it up into the air and let the pellets rain down and maybe it catches somebody accidentally, that's not good enough, but that's the basic idea.

Baker: Well, we'd better move along. Well, I assume then that you agree that some foundations were laid for molecular biology and for biotechnology?

Boone: Everybody does.

Baker: Well no. Not everybody.

Boone: Well then, let me outline it quickly. Okay? Our oncogenes, our DNA research, our molecular genetics, our molecular biology, the code, DNA-involved research, all of this, got a tremendous boost from the Virus Cancer Program, and I think most people will agree to that. It stimulated research on the majority of fronts that we are looking at today in terms of cancer research. And I can pick up any *Cancer Research* issue that outlines some meeting and point out that most of the topic headings can go directly back to what the Virus Cancer Program did, give or take a few.

Baker: I'll turn now to a broader philosophic question, and this is the public's perception of science in general, not just biomedicine even. Do you think the public is more aware of science and understands it better today than they did in 1965, or the same, or worse?

Boone: I would say there was a copy of *Life* magazine with a picture of Huebner looking like a St. Bernard shaggy-dog and he had these woeful eyes and, at the bottom it said, "Will this man find a cancer virus?" So, the public was much more aware and excited, in my opinion, in those days because they had something they could understand. Today, we're back to the idea that the average person now is cynical because he's seen too many reports in the news reported by the media who want to sell newspapers and influence events, but mostly sell newspapers, too many reports by people who only have half, or less, knowledge, who may be sincere in their claim, but these claims are only a small part of the picture and never give anything that's rational they can really sink their hands into. It's always pap, always something superficial.

Baker: Does this include some scientists?

Boone: Many scientists will make a statement through the media which is very well meaning but the public is cynical because these are only preliminary results and we don't want to make too many inferential leaps, and so they take it with a grain of salt and they have somebody's idea today and somebody else's tomorrow. And the news media always tout it and makes it bigger than it really is. So, they're just tired and cynical and they're waiting for something substantive. That's what I think.

Baker: Do you think this affects the funding of science, or will it?

Boone: I think the nature of the human race is to ballyhoo and beat the drum to get funding, so I think that will never change. That's the way it is.

Baker: Well, in the cancer field, at least, people are frightened enough of the

disease that funding is probably going to continue in that area.

Boone: Well, the fear lever is one of the chief reasons why we're all funded as well as we are.

Baker: Any additional comments you'd like to make before we terminate this?

Boone: No. It's been much more fun than I ever thought to share these ideas.

Baker: Well, reminiscing is fun if you had a good life, like we had.

Boone: Yes, it was. This is my final thought. If only we had the funding and the wits and the courage--the *cojones*--to find another topic and do it again. That's my final word.

Baker: Very good. Thanks very much.

Conclusion of Interview