

Dr. Ruth Kirschstein, Deputy Director of the National Institutes of Health
The interview is conducted in Dr. Kirschstein's office at the NIH
17 March 1999

Interviewers: Dr. Victoria Harden, NIH Historian and Dr. Caroline Hannaway
Please Note: These interviews have not been verified for complete accuracy

Harden: Dr. Kirschstein, to start this interview, I would like to go off on somewhat of a tangent and ask you some questions about the recent publicity surrounding the Salk polio vaccine and whether the SP40 that contaminated it before 1960 might be causing malignancies today. The report that gained publicity on the news was essentially the information discussed in the conference proceedings that you gave us in session two. But I wanted to hear you comment, if you would, first, on the substance of those arguments; and second, on what you as a federal employee and a scientist who has dealt with polio think about the responsibilities of scientists and the press in publicizing things that could cause a lot of public upset.

Kirschstein: Although to some extent the report was based on the conference that I described to you, what actually happened was that a woman who had worked in the field for a long time, named [Dr.] Janet Butelle, who has been associated with [Dr. Joseph] Joe Melnick , and is still down in Texas, at Baylor, wrote this review article in the *Journal of the National Cancer Institute* [published]January 20 [1999]. Probably because of the conference, what people thought she said in this article got picked up in the press. Now, I have not talked to Janet. I have known her for years, but I have not talked to her, nor do I know anybody who has. But subsequent to the original first report, she was concerned enough that she spoke out and said that the press had not interpreted what she said fairly. I have read the article once. Several people I know have read it more often, and I want to read it

very carefully again. You can see, the instant I heard what you were talking about. She has data in there that has some suggestion of plausibility. But neither she nor several of the rest of us feel that the way the press went about this in the first press articles justified the conclusions that they drew. What I hoped would come out of this article is that there would be continued study. When we first made our discoveries, Bernice Eddy, I, and others, that SP40 was a tumorigenic virus in hamsters, we worked very hard to look and see whether you could do the same thing in primates and in other higher mammals, and you could not. There have subsequently been some SP40-like viruses, JC and something B—I cannot remember the first letter—isolated from brain tissue of people who have been markedly immunosuppressed, and there have been some reports, maybe yes, maybe no, of association with tumors. It is still a very murky area, and I do not think any real conclusions can be drawn. It has been many years now since first the Salk vaccine and the beginnings of the Sabin vaccine were given. There certainly has not been anything that could be called a catastrophe. There has not been anything that could be called absolute in any sense. Whether or not, under circumstances that we do not all understand, an occasional situation like this arises, I think is what Janet is talking about and what more people need to look at. [Dr. Joseph] Joe Fraumeni, who is the director of the Division of Epidemiology in the Cancer Institute, did study and wrote a paper, which I think he published in the AMA Journal—I cannot remember where—on following the cases, and he could not find anything. Now, I have not—and probably should, but I just have not had time—talked to Joe since Janet’s paper came out. He would be worth

talking to about that. On the other hand, I do think a federal official needs to be very careful. We do not want to panic anybody. We have eliminated polio in this country. We hope to eliminate it in the world. We do not want right now to stop people from getting vaccine. We do not want to have a panic. And we also do not want to suppress science. The whole business of SP40 in its initial phases and why things happened was because the original Bernice Eddy paper was suppressed by—he is dead so I can say it—Joe Smadel. We do not want to do that. In the worst way, we do not want to do that. On the other hand, we do not want to go too far the other way. So we have to strike a balance, and I think that, particularly, the people who work for the federal government have a public policy position of being careful and honest.

Harden: I was struck by two things. One, I do not believe the author of the article in *JNCI* did realize just what the press might do with the material. Two, I was surprised that it struck such terror into people. A senior female administrator at George Washington, who is not known to fly off the handle about things, called me very upset, saying, “Will my children get cancer if they had this polio vaccine?” So these medical questions strike sensitive things [areas], is what I have been getting at.

Kirschstein: One other thing. Polio has been something we have not talked about much in this country recently because there has not been any need to. Whether the fact that there was the recent PBS television program, which was the one that I saw originally as the movie down at George Washington University—I wonder if the woman you know was in the audience at that movie—has brought polio back to

people's minds, and therefore when this happened, there was more concern than one might have expected. We will never know, but it is a possibility.

Hannaway: Because there is not only a TV program, there is also a book with a lot of pictures and so on.

Kirschstein: Yes. Actually, the book, I gather, was a result of the TV program.

Hannaway: Yes. But some people have seen the book even if they have not seen the movie.

Kirschstein: Yes, that is possible.

Hannaway: A second question we have added to the list also relates to polio and vaccines. Yesterday, the *Baltimore Sun* had a front-page article on the Surgeon General's recommendation that the Salk killed virus vaccine be the vaccine of choice instead of the Sabin live-virus vaccine, because of the risk of infecting unvaccinated individuals with the Sabin, and also because some people got polio from the Sabin vaccine. Would you comment on this recent news?

Kirschstein: We have come full circle. Each type of vaccine, as I told you when we first started these interviews, has its place. Until we were sure that the live attenuated vaccine would not only, which we knew, immunize the vast majority of the population but also would not cause more than about one [case of polio] in 300 or whatever it was thousand people, the better part of valor was to use the Salk vaccine. Now, the Salk vaccine in those days was not quite as potent as it should have been. We talked about that before. That meant that if polio was still extant in the world, or in the country, one would have to boost people fairly regularly. The Sabin vaccine, which was the final choice and which really was remarkably safe, did cause an occasional case, or at least it seemed like it did, and I think the evidence

is pretty good. Once you have gotten to the point where there is no disease, then even those rare cases are more than one should have to deal with. Vaccination basically is a public health procedure—I have said that before—to protect the public's health at large. As long as that is the aim, then you take an occasional chance. Once you have gotten to the point where it is evident that the public-at-large is protected, then you should change your strategy and protect everyone. Now, it remains to be seen whether or not the Salk vaccine—I presume it is, but I have not followed the recent events—is more potent than it was before.

Hannaway: They call it the enhanced Salk vaccine.

Kirschstein: Then it almost surely is. I think I told you that I thought that the best possible thing—but you cannot do that in a public health way because it is too expensive—was to use them both.

Hannaway: Now we would like to go back to where we were in the questions last time about your NIGMS career. We were starting to discuss the two research training programs, the Minority Access to Research Careers that was formally established in 1975, and then the Minority Biomedical Research Support Program and the Medical Scientist Training Program. We would like you to describe each of these programs and the problems and successes that you had with them.

Kirschstein: Both the Minority Access to Research Careers Program and the Medical Scientist Training Program existed in a very small way, each of them being very small programs, before I became the director of NIGMS. The Minority Access to Research Careers Program was established under the advice of a woman who was probably the first African American member of an advisory council at NIH, Dr.

Geraldine Woods. Geraldine Woods had gone to Radcliffe—rather unusual in those days—and actually went on and got a Ph.D. in biology at Radcliffe, though it probably was awarded through Harvard. I do not recall. It was in the 1960s. She never then did science herself, which was too bad. She married a dentist, and she began to do “good work,” philanthropic work, things to support in many ways the minority community. Now, this was, of course, at the height of the civil rights movement. She knew Martin Luther King very well. She knew some of the others. She became very interested in what could be done to educate minority populations better scientifically. She took as her cause doing something to enhance the scientific activities of the historically black colleges and universities, the HBCUs. She started this with the blessing of Dr. Robert Stone. First, she did it alone for a while. Then, in 1972, after Dr. Marston resigned, the next director was Dr. Robert Stone, and she and he and Dr. [Frederick] Fred Stone, who was the director of NIGMS originally, began to visit historically black colleges and universities, and they took some of the NIGMS staff along. They set up the start, in 1972, two years before I went to NIGMS, of the Minority Access to Research Careers program. It was an individual fellowship program for young men and women who had one way or another gotten their Ph.D. degrees at what were the only three M.D. or Ph.D.-granting HBCUs at the time, Meharry, Morehouse Medical School, and Howard. And how could we support them? They developed a program of individual fellowships. When I got to NIGMS in 1974 and studied the issue, it seemed like a terrible snail’s-pace way to go—with only a hundred fellows a year, maybe less-- we would never make any progress. Unfortunately,

we still have not made enough yet. But it did occur to me, and I brought a group of advisors in, that one of the ways to entice more minority individuals, particularly from HBCUs—HBC is the undergraduate part of the HBCUs—was to be able to support them in their college years, particularly in the junior and senior year, try to get them into science, support them in a science major, and then help them try to get into graduate school. Now, we got that advice from a number of people. The department at that time was not the Department of Health and Human Services. It was the Department of Health, Education, and Welfare. Education was part of our department, and they firmly said, “College education is none of NIH’s business. We do education.” We were supposed to do health things—research training for health, and so forth. Their lawyers said that primarily, and they were to some extent defending their own turf. We then began to write a series of papers that explained that we were not interested in “education” as they conceived it. We were interested in a continuum of “research training” that would prepare the students so that they could go on to a graduate degree. We designed the program with curricula, with working in laboratories while they were going to school, with a summer program that hopefully would put them full time into research between the sophomore and the junior year, and between the junior and senior year, and on when they graduated almost immediately. We finally got concurrence from everybody. The health part, the secretary, presumably education signed off. I never met very much with those people. Now, when we started that—Geraldine Woods was part of the council and she was pushing us all the way—I asked some of my most valued scientific and educational colleagues at

HBCUs, all of whom had had experience in HBCUs, how many of the 110 or so HBCs that there were would be able to mount such a program of a worthwhile quality. Most of them said somewhere between 15 and 20. So we started off with 11 the first year, 15 or so the next year. But what none of us realized was that, if you opened the door, you could not limit it to 15, you could not limit it to 20. You could perhaps prevent it from being 110, but it quickly grew to about 90. That meant that there were a lot of kids going through getting science coursework that was not as good as it should have been, and that would have been no different than if they had gone to a fairly small rural college in the west, in northwestern states, etc., or some of the southern non-HBC schools. The difference was that the young people from those other colleges, if they did not get to graduate school where they wanted to go, could go almost anywhere and enhance those educational possibilities. It was much more difficult, if you were able to do it at all, coming from an HBC, at least in the early or mid-1970s. Secondly, what we should have realized, and did not, was that for students who were probably in some ways the very first members of their family to go to college, other than to become teachers—we talked about normal schools before—their parents would say, “You are going to have to make a decent living, and I do not know whether you will be able to do that with a Ph.D. in embryology. I do not even know what embryology is. Why don’t you go to medical school?” Also non-HBCUs, there still being only three HB medical schools in this country, were beginning to take more of these students. So we succeeded in doing what we thought was an anathema--we were wrong--and that was to increase the number of physicians of

color in this country, but not really increase the number of researchers. Now, you can argue—and we did—that [because of the program] they understood research better than would doctors who had not had some research experience. You can argue that some of them with M.D.s did go on to research careers. The numbers were not very substantial. And depending on the friendliness of the members of the congressional Appropriations Committee, we were always being asked to evaluate the program, and the data were really pretty loose. At the same time that Dr. Woods was working with NIGMS, she was also [working with another group]—she did not like this idea of an elitist program that was going to be only 15 or 20 schools. All she was really interested in—from her point of view, quite legitimately—was getting more money to those schools. A research training program was fine and dandy, but it was not going to do enough. So there was the then-called Division of Research Resources—it was a group that I had told you was part of NIGMS and they split away and were supposed to sort of help infrastructure. So she went to them. Everybody at NIH was trying to prove their worth in those days as to what they could do to improve the situation. It was bad. She got them to set up the Minority Biomedical Research Support Program, which basically was an institutional grant, free money. It was do research, do not bother reviewing it very much—I am being a little bit provocative—and students to work there. There was, before and even after I came, a rather difficult rivalry between the people in NIGMS who ran the MARC Program and the people over at DRR who ran the MBRS program. She loved playing them against each other. It did not help anybody. In point of fact, the MBRS program quickly got the

reputation of just what I said, a program that was not of great substance at that time. The way most of the money got into the MBRS program was for the other institutes to add money because DRR did not have a lot of money. The grants, whatever they were like, would go to the various councils of the other institutes. The councils would look at them and they were almost afraid to say no. This went on for some time, and I think I told you—I do not remember—that there had been a number of studies about NIGMS and DRR and whether they should be combined after I became the director.

Hannaway: Yes. You touched on that briefly.

Kirschstein: There were several studies before I arrived, but there was one that started the day I walked in the door as director of NIGMS, and there were about three afterward. But the one in 1988, which was engendered by some unhappiness that Dr. Louis Sullivan as president of Morehouse Medical School had, starting about three months before he became the Assistant Secretary for Health, led to Dr. Wyngaarden and [Dr. William] Raub setting up another study. That one ended up with a whole series of recommendations which would essentially have put the then Division of Research Resources out of business and transferred the majority of its programs to NIGMS. The one program, General Clinical Research Center's program, would have gone to NI—I think it was DDK by that time. It may have been NIAMD, but I think it was DDK because it was clinical. In the end, just as every time before, the director of NIH, Scott _____[?], said, "I cannot do that, with one exception. I will transfer the MBRS program to NIGMS to join the MARC program so that we can have an integrated whole." It has been 11 years

and they have not had an integrated whole yet. That is because of turf. Now, they have done a very good job, and we did a very good job before I left, of beginning to integrate them to keep the identity of the two programs somewhat separate. What I did—and they have carried it forward because it happened just before I left—was to make an umbrella program, Minority Opportunities for Research Program, MOR. It was a nice word: You need more. They then placed the two bits under it, hoping that gradually they would integrate. I think it will take another generation [for that to happen]. But it is much better than it used to be, and the quality of the MBRS program has improved as a result. They have finally done the evaluation, and what you find are several things—they did not have to do the evaluation to come to this conclusion, but it, at least, had data. HBCs that had either never had decent science curricula, or had had poor science curricula enhanced those curricula. They were much stronger as a result of the MARC program. The number of HBC student attendees, enrolled students, who majored in any sort of science, but particularly a biological science, increased by very substantial numbers. The number of HBC graduates who went on to non-HBCU medical schools increased greatly. It had been started before. The number of African American or any other minority, because we quickly decided we could not concentrate only on HBCUs and we had Hispanic-serving institutions and then we had this whole series of institutions, City College in New York, one of the universities, NOVA, I guess, in Florida, UCLA now, which have large numbers of minority students—City College is very different than when I was a girl growing up in New York City—they added to the program. The vast majority

of the students went to medical school, and we stopped saying it was a crime. But the number of biomedical researchers has increased infinitesimally, if at all, recently. The National Science Foundation keeps records. When you get your Ph.D. in science, you are supposed to fill out a graduate record form. I guess that is implemented pretty well because the vast majority, probably 90 percent, of students do fill out the forms and send them in. Then NSF collates them and does all sorts of things with them. In fact, the number [of minority researchers] is beginning to fall off now, unfortunately.

Hannaway: Just as the number of women is falling off a little, too.

Kirschstein: In graduate school?

Hannaway: Yes.

Kirschstein: I did not realize that.

Hannaway: I mean, who are going into research.

Kirschstein: I did not know that. But I think it is going to take more time than I ever anticipated. You may know that Harold [Varmus], just six or eight months ago, put together a committee headed by Harold Slatkin, who has called for NIH to set up an academy for minority students. Everything that we ever did is [repeated]. We reinvented the wheel, but nobody believes it, so, I sit and watch with interest. Now, the MSTP program, Medical Scientist Training Program, is a combined M.D.-Ph.D. program. Our department, and the federal government generally, does not support, other than through things like the GI Bill, with outright support—there may be scholarship support, but not outright support—medical students or dental students to go to medical school and then go out and practice

and make a lot of money. That is considered a no-no. I think there are even some regulations against it. Dr. Shannon, when he was director of the NIH, knew that he had become the researcher that he was, not because he went to medical school—medical school, I think I said this, is a trade school—but because of the Ph.D. he got afterwards. He realized that medical students needed to learn how to do research. He thought it was very important that there be M.D. researchers because they brought [a] sensitivity to the field that perhaps others did not. In the case of an individual such as Arthur Kornberg, who has only an M.D. degree, he could bring that, but he was a natural researcher and trained here for a number of years before he went on to his great career. I think people here will tell you that they saw all the glimmerings of that great career while he was still here.

Dr. Shannon, who basically set up all the research training programs of NIGMS—Fred Stone had worked with him and he basically told him what to do—planned the M.D.-Ph.D. program and the Medical Scientist Training Program. It actually started in 1965, so that was nine years before I became the director. It started with three schools. They submitted applications and they were peer reviewed. You kind of knew which the schools were going to be before the program started: NYU, Einstein, and the University of Pennsylvania. The program gradually expanded, so by the time I got to NIGMS, it was 10 schools or something like that. It took schools a while to be able to develop this kind of program. It is not an M.D. and then a Ph.D. It is an integrated program where the students, in their first year of medical school, take medical school lab courses and an enhanced set of things. They can place out of biochemistry if they have taken advanced

biochemistry in college, and go on to some of the graduate schools. A little more of the same in their second year, though the students begin to do rotations in laboratories to find out what they want to do their thesis on. They do lab work for the next several years, going back and doing physical diagnosis and seeing patients and so forth. Then they go back and finish up whatever they have to. Since most medical schools, in the fourth year, allow students to take electives almost entirely, most of the students could then continue to work on their research as an elective. They end up getting the M.D.-Ph.D. degree, usually taking between six and eight years, which is to some extent double the other level, but there are really first-class students going in and doing remarkable work. The program pays their tuition, just as you pay tuition for regular training grants, and a stipend and whatever else, some of the benefits. But, instead of paying, as for graduate students, about two years of tuition--because graduate students stay in course work for a year or two and then go into the lab. Then they are paid on a teaching assistantship or a research associateship or whatever--we were paying six to eight years of medical school tuition—a very expensive program. However, when you look at the data that come out of that program-- they just recently did finish an analysis--these are the most successful NIH grant recipients. Their success rate exceeds that of other Ph.D.s. Their achievements exceed [those of] almost all other scientists.

Harden: You mean the fact that they do go into research.

Kirschstein: They go into research.

Hannaway: Do they publish a lot?

Kirschstein: They publish a lot, they go into research, they are eminently successful researchers. We have nine of them here at NIH. We had nine; I think it is more now. A number of them are laboratory chiefs, a number of them are really outstanding people. The problem is, from the point of view of an individual who believes that, with the M.D. degree, they ought to do something that is related to medicine, that they should become clinical researchers. There is a man up at Rockefeller, Edward Ahrens, who is furious. He thinks it is a terrible waste. You are not teaching the students anything that they can use valuably in thinking about patients. It turns out that most of them, because of the genetic and molecular biological revolution, are doing molecular biology and genetics. That is where the research opportunities are the greatest and they can make the most important discoveries. Nevertheless, they are not doing those activities in departments of biochemistry and microbiology. They are doing them in departments of medicine, pediatrics, occasionally surgery, occasionally one of the small surgical specialties, but basically in medicine and pediatrics. They are taking their turn in teaching in those departments, and they are taking their turn in going on rounds and teaching students at the bedside. So I would argue, and I think a lot of other people would argue, that this has been an eminently successful program. We have had, the same way as when you open the door, to expand the program. It grew to 22 [schools] in the first few years that I was at NIGMS. It grew to 29 shortly before I left. I guess it was 31 when I left, and I understand it is up to 35.

Harden: Institutions?

Kirschstein: Institutions, medical schools.

Hannaway: Have received these grants?

Kirschstein: Have received these grants. They are institutional grants. They are monitoring them carefully to see [what happens], and they do undergo, I think, the most stringent peer review that I have ever seen. Each one of those first three schools, Penn, NYU, and Einstein, had grants of five years. By about 1979 or so, every one of the deans of those medical schools was in my office because they had become so self-assured in this wonderful program that they had had that the reviews showed that they were no longer of the best. They became complacent, and we almost stopped them. It was hard to do, so we gave them a year's grace. They all came back and learned their lessons very well because they are basically wonderful schools. It was just that they were not paying enough attention.

Hannaway: They were taking things for granted?

Kirschstein: Yes. They were. And that is true several times.

Harden: But you have data now that show that people who start this program do indeed finish the M.D. as well as the Ph.D.

Kirschstein: Yes. There were a few who dropped out of either degree. One of the classic examples works here on the NIH campus. It is [Dr.] Sylvan Green in the Cancer Institute, who started out in the Penn program and very quickly realized what he wanted to do, was real epidemiologic research. He started to do that and did not bother working on the Ph.D. courses. He is considered one of the whizzes around here. I do not consider that a failure. A couple of them who decided that they did not want any part of this trade school aspect of medical school, dropped out, and ended up with Ph.D.s are doing extremely well. They are not counted in the

program, nor is Sylvan, but I do not call that a failure either. The vast majority do get both degrees. The program was, unfortunately, until relatively recently, very heavily male, because when you get through medical school and then go on to your residency training, because almost all of them, although they do research, do take specialty training, residency training. If you can get out in four years get your residency training, as a woman, you have a chance to think about whether you can combine career and family. If it takes you eight years to get out and then do the rest, it becomes more difficult. It has been a little less so recently as women have learned how to juggle things better. The second thing is that, in hard times, as in the budgetary era of the 1980s, we found that this eight years of medical school tuition was beyond what we could do. So we limited it to six. The school was going to have to find a way, and it did, to take care of those who could not finish in six years. But it is a remarkably successful program, and that is the vision of James Shannon.

Hannaway: Just to follow up one point about this, you mentioned that the program is subject to very vigorous peer review. Has there been any difficulty in getting congressional approval of appropriations for this program?

Kirschstein: No. Not for the MSTP program. In fact, they kept asking us to increase it more rapidly than we wanted to. The AAMC had done some analyses. Jim Wyngaarden had written this paper called "The Clinical Investigator: The Endangered Species." He was wildly enthusiastic about it. The person who has been the least so in one way, but not in another, has been Dr. Varmus, because he saw the program, one of the very best, at the University of California-San Francisco, and

he knew that they all did molecular biology. He is trying to push people into clinical research these days, and he thinks there are other ways to do it. He has balanced it out, but, on the whole, I think he thinks it is pretty good.

Harden: Let me ask one follow-up question here on a topic that you certainly mentioned, and this is the ongoing problem that, despite all these efforts, the number of minorities and women [who are biomedical researchers] still lags behind in proportional numbers. Now, in your view, is this just a matter that we need to keep plugging away at trying to support this, or is there another problem that needs to be dealt with another way?

Kirschstein: There are two problems. The number of women enrolling in medical school these days, each class is somewhere around 40 percent, and some classes have 50 percent. The number of women in graduate school in the sciences, not in all the sciences but in the biological sciences, is also about 40 or 50 percent, so there is no lack of them. In the case of research training for the Ph.D. degree, the number of women who end up being successful in getting research grants is smaller than the number of men. Part of that, we think, is related to the whole issue of tenure and tenure track at universities. Part of it is related to the thing I talked about before, which is if they get married and they are married to other researchers or academicians or even businessmen who move to a different place. It is more common now, from what I hear, for there to be commuting marriages. I do not know how you do that, but that is okay—that is a personal philosophy; Vicky knows, you may not, but there is nowhere that I go, even to dinner, that Al does not go and vice versa. We are very, very close.

Harden: Joined at the hip, I think it has been said.

Kirschstein: Yes, joined at the hip, and we love it!

Hannaway: I think that is a good philosophy of marriage.

Kirschstein: Right. But there is also beginning to be more sensitivity at universities for helping this situation along. I remember talking at a conference of Dr. [Vivian] Pinn, whose office has sponsored a number of these conferences, and I talked at one of them. Then one of the deans of a medical school got up and said that when one of the spouses comes, they have recruited him or her, and says, “I need to have something done for my partner,” if that individual is in a medical or biological science, he, the dean of the medical school, can call up various people and find a position. If the individual is a historian, he, the dean of the medical school, does not have much clout with the dean of the college of arts and sciences, or even the department of history, and it becomes a more difficult problem. We have not quite solved that yet. Women who are good scientists have been spectacularly successful. Last night I went—I do not go often—to the meeting of the local chapter of American Women in Science, which was over in the Cloister on the first or second Tuesday of the month. Ellie Ahrenfeld [sp. phonetically] spoke on “how to land a career in academia.” There were a large number of postdoctoral fellows there, mostly women, and she gave them some hints about how to go about things. She told me an interesting story, which was—it had come home and hit her—that her daughter has just finished her master’s in public health and was looking for a job. The daughter went to the Internet and found various possibilities, and one of them said, “You can submit your application by e-mail.”

As she began to fill out the application, there was a question about what salary do you want, and she panicked and called her mother. She said, “I do not want to ask for too much, and I do not want to ask for too little. I do not want to seem an indecisive woman, but I do not want to seem like somebody who thinks she is better than she is. What should I do?” And Ellie said, “You have a boyfriend. He has a job. Why don’t you ask him what he did?” So the daughter did, and she found that he is now working at a \$30,000 job, and when they asked him, he said \$50,000. Ellie said to her daughter, what you did was a typically womanly thing. What he did was to say what he would like. He knew he was going to have to come down. I am not sure I would have gone to \$50,000, but pick a number that seems reasonable and do it. And you will talk to them. If they really want you, that is not going to be the breaker right now, unless you ask for a million dollars or something like that.” So women do need pointers in that regard, some more than others. Some women need mentors. I never had a mentor. I never felt the need for a mentor. But I have mentored many, many women and men too. But women probably get discouraged more easily than do men, and if they do not succeed quickly, they will find something else. Our extramural programs here, the programs that have the grants managers, are much more heavily female than male, for all sorts of reasons. One, it allows them to have a lifestyle that involves family more. Two, they seem to be able to get what I think is absolutely the critical element of being a good health sciences administrator; scientific satisfaction, and helping somebody else do science rather than feeling that the only way I can do this is if my ego is satisfied that I do it myself. The story is very

different for minorities. That is one that I really do not know what we should do about. First of all, you cannot say these days that the women are being truly discriminated against in terms of graduate schools, in terms of finishing up, in terms of getting doctorates, postdocs. The data even show what I wrote in the article in the *New England Journal of Medicine* about pay becoming better. We are not there yet, but it is becoming better. Of course, many of these women come out of families in which parents and perhaps grandparents as well, as for the majority of white males, not all, go to graduate school or medical school. These families feel that education particularly higher education is very important and the parents have either [a] bachelor's degree, at least and maybe more than that. That is not true, with rare exceptions, for the minority population. There was an article, I think, either in the *New York Times* or the *Washington Post* this past Sunday about the very upper-class African Americans, but that is a very small group. It is growing, but it is a very small population. The couple of times that I have given commencement addresses, for example, at Mt. Sinai Medical School in New York, which has a very mixed population of medical students—Hispanic, both from Cuba and Puerto Rico, some of the South American countries; African Americans; Indians from India; Pakistanis—for most of those students, it is the first time that anybody in the family got a bachelor's degree, no less a medical degree. And I sat there on that stage and watched as the students paraded across. Parents and sisters and brothers were screaming with joy and rushing up to take pictures. "I'm going to send them back to your grandparents in Puerto Rico," or whatever. The idea that your child could achieve that was almost unbelievable to

them. And for black Americans as well. Plus, I think we have to face the fact that we still, in our academic institutions, particularly our great academic institutions, and I will include NIH—they know it here as well; you and I had this experience. Were you there also that day?--the intramural NIH program as saying, if you are not the very best, we won't consider you, and making no attempt to say, "Well, look how much he or she has achieved. We want to give them a chance." No, no. If I want to pick between 5.0, no, 4.0 at Harvard, a Ph.D. at Harvard, versus 3.8 at G.W., African American, I won't pick the G.W. person.

Harden: It is always interesting to me as to what constitutes the best. I think it has generally been defined as either a test score or a grade-point average. I know from talking to a lot of intramural scientists, for example—and I am sure this pervades academia as well—that it is the sense of innate brightness that impresses people. Of course, in so many things, just being the member of a certain group or class, a certain whatever, has been the entree, whether you have the grades or not. So it is a matter of making policies, is it not, about who will get that marginal—

Kirschstein: We are beginning to change. I had this young man who was in the undergraduate program that Mark Hurowitz [sp. phonetically] runs. The name is Jose Varga [sp. phonetically]. He just won the Rhodes scholarship. He was written up as a Rhodes Scholar. Well, he came from Guatemala. I think that is where his parents were from. Loyola College in Baltimore is not exactly Ivy League but it is very good. It was the first time that Loyola has ever had a Rhodes Scholar, and he was probably written up in the Baltimore newspaper.

Hannaway: He was.

Kirschstein: Not only that. Before he ever knew about the Rhodes, he had won the Marshall scholarship, which is pretty much the same. He is going off to Oxford this July to work in a prestigious laboratory in genetics with a wonderful geneticist. What they get over there is the D.Sc. He has been admitted to Harvard Medical School, and they will defer him for the three years that it will take him to get the equivalent of a Ph.D. in England. He could not get that in this country. He came to the U.S. at the age of 13. He speaks English without an accent. It was one of the most exciting experiences of my life to talk to him. Now, some of the people in the intramural program would say, “He did not go to Harvard, so he doesn’t rate.” So we have to change that. I do not know how. Michael Gottesman is committed, a number of others of us are committed, but he has got to get that group of people you were talking to that Wednesday morning [to be committed]. They are the biggest—

Hannaway: The most recalcitrant?

Kirschstein: Well, no.

Harden: They open the door.

Kirschstein: Intellectual snobs. Isn’t that true? You will not say it because you have to deal with them. I know that. They know what I think because I tell them that. And they say to me, “Wouldn’t you do the same?” I do not know, I doubt that I would, but I am not sure.

Hannaway: There is one group that wants to make a notable investment in its children vis-a-vis education and careers, and those are the Asian Americans. When I go to the Hopkins campus and look around at the undergraduate body, half of the students

now are Asian Americans.

Kirschstein: That is right. The Asian American immigrants to this country—including Vietnamese and so forth—intellectually are in the same position as the Jewish immigrants in the 1890s and early 1900s. But they had a culture of intellectual ability, the parents thinking if they themselves did not go to college, the children would. That is thousands of years old. Unfortunately, we do not always have that from very poor Hispanic populations and from people who came to this country in chains.

Harden: But what you are touching on is the kind of politically explosive topic as to whether you can characterize cultures.

Kirschstein: Yes, right, it is, and I am not going to judge. But there is another point that I want to make that goes with what you have been saying. That is that we do still have, of course, the other aspect of things, which is overt discrimination. We are ending this with a number of years of integration and affirmative action with Supreme Court decisions, and with other court decisions. An interesting thing happened just the other day, March 4, when Harold and I went to testify in front of the House Appropriations Committee, and they asked us about some of the programs. Dr. Griffin was with us. Harold made a statement about some of the things that are needed to increase the population [of minorities], and he used—I cannot quote; the transcript will come and I will see it—the term affirmative action. The congressman from San Diego, California, Cunningham, stopped him and said, “Not affirmative action, Dr. Varnus. I will fight you to the death on that. Affirmative access, yes.”

Harden: Interesting.

Kirschstein: Yes. Harold's point was related to the fact that if we really want to increase the number of minority research physicians, then we need to have the enrollments at medical schools stay the way they have been. Indeed, what is happening with the California Proposition, is it 209, is that the students are not even applying now. So the enrollment, the application rate for minority students has plummeted. They do not want to go where they know there is no chance. That was what he was saying to the congressman. So there was a very, very—

Hannaway: A changing political climate.

Kirschstein: I do not know quite what to do about this because we are having problems here, being sure that we will be able to keep programs like this going. Now, the great piece that I think I forgot to mention as part of the MARC program was that I always felt that as long as we had to confine the program to the HBCUs and the Hispanic-serving institutions, we were not really doing what we needed. We wanted to support more graduate students who were considered to be minority students at the Harvard's, the Yale's, and the Universities of Michigan and Chicago, etc. So we set up an individual MARC pre-doctoral fellowship at those schools in about the last two years that I was director. So it would have been 1990, 1991, 1992, somewhere in there. We knew that there might be some problems about picking special people who let the institution declare that they were picking minority students, and if they wanted to pick somebody who was not, we did not argue with them. That is a program that is probably going to be vulnerable to the decisions that the Supreme Court has made. In my view, that is

very sad because there you are saying that these individuals get an opportunity to see the very best when they cannot always see it elsewhere. I do not know how it is going to come out. If you had told me in 1974 that we were going to have as little effect on the number of minority investigators as we have had, I would not have believed it. I would have thought we would have done better. It is one of the great disappointments of my life.

Harden: It is a knotty problem.

Kirschstein: I have gone on much too long.

Hannaway: No. That is fine.

Kirschstein: I do not mind.

Hannaway: All right. Let us come back to some of your considerable other activities as well as directing NIGMS. You sat on the National Committee on Diabetes in 1974; and 1977 through 1982, you were on the Fogarty Center Scholars in Residence Advisory Committee. Could you tell us a little bit about the functions of these groups and what they accomplished while you were a member?

Kirschstein: I will talk about the Fogarty afterwards. The Diabetes Committee was one that, by law, the Congress ordained that every institute director would be a member of, along with a whole series of other appointed individuals. It was the start of this continuing drum roll that we have had since 1975 I guess, to increase the funding for diabetes. So, every institute director was a member. I did not go to all the meetings. I went to important meetings. I probably had no particular role in that. It was something you did.

Harden: Let me follow up on that. My memory is that there was a period in the 1980s, and

maybe it went back earlier, when the Congress was asking for these kinds of participation. There would be subject areas they wanted across all the institutes.

Kirschstein: Diabetes was the first one. Then there was an arthritis one. There were others. Yes absolutely. They saw that as a way of satisfying the constituent groups. In point of fact when the money did not increase remarkably, that did not seem to be a way. The commissions or the committees or whatever they were called were in the law, and it was only in 1993 or 1994 that, by writing a letter to Congress, we were able to get rid of a number of them. In fact, the constituency and advocacy groups have found that they could do much better by going to the Congress and beating on members. That is what has been happening, particularly with diabetes. You have seen stuff with things that are coming out, and you know that there has just been a Diabetes Working Group headed by Ron Conn [sp. phonetically] from—he is either at Tufts or Harvard now; I do not remember. He used to be here—and put in law that there should be this group, by George Nevicut [sp. phonetically]. They have a report, and they are asking for fantastic amounts of increased money for diabetes in the next several years. Other groups will come along and do the same. It is also those advocacy groups which have caused us to form—and, of course, the IOM study--the new group that Anne Thomas has to put together, a council of public liaison or public representatives. This is a new era.

Harden: We will continue this conversation another time, too, because I have lots of thoughts on this.

Kirschstein: So does Anne and so do I. We do not have much we can do about it, however.

Hannaway: Can you tell us about the Fogarty Center committee?

Kirschstein: The Fogarty Scholars in Residence Program was—I do not know much about it in the 1960s, when I was in the laboratory—in the 1970s and early 1980s, quite a remarkable program. We had wonderful scholars from abroad who came here to think and have time off to do things. In the early days of that program, they lived in Stone House. They had sort of suites for them. They ate many of their meals together. They invited scientists from the campus to meet with them. It was elitist. In general, they always had only intramural scientists as part of the review group and the advisory group. Either because when they did that, they had, I think, white males sitting around the table, or because the people who ran Fogarty, and I do not know which, genuinely believed that the time had come to expand this to scientists in the extramural programs here, they invited two women to join the committee in whatever year it was.

Hannaway: Seventy-seven.

Kirschstein: Seventy-seven to 1982. One was Claire Winestock, who was an executive secretary in the Division of Research Grants and who ran this virology study section. For reasons that I do not know exactly, the makeup of the Fogarty Scholars was very heavily virologists. I was the other woman. We did a lot of worthwhile things. We reviewed the applications we talked about the kinds of people who should come, etc. The Fogarty Scholars Program does not quite exist anymore. It got to be a very expensive program, and it turned out that the institutes did not much care. So Dr. Varmus made a decision that if the institutes wanted a scholar they wanted to call Fogarty, they could bring somebody over and pay for him or her themselves. In recent years, the scholars have not been

living in Stone House. It was Hans Stetten, I think, who said, “Why should we be running a hotel?” or something. Maybe it was not Hans but somebody over there. But somebody said NIH is running a hotel and we should not be in the hotel business, and we had some problems with the people who were running the hotel. So then we had the scholars living either off campus or in the apartment house. Well, we knew the apartment house was going down, so things have changed. I do not think that was a policymaking committee. It was a review committee, and I enjoyed it.

Harden: To follow up on this, what is the Fogarty Center doing these days? If it is not funding scholars coming here, is it funding grants to scholars in other countries or funding people from here going to other countries?

Kirschstein: It is doing a little bit of all those things. The scholars would be sort of senior people, and that is not going on so much. The Center is involved with many of the young foreign people who are here. Dr. Varmus is trying to increase the amount of activity that we have in relationship to international health. Actually, he and the Secretary talked about it the other day when I was there, and Congress is very interested—not all of Congress. Mr. [John] Porter is very interested in this, and particularly because we have a new, dynamic director of the WHO, Gro Brundtland. We have a new director of the Fogarty, too, as you know, Jerry Kirsch. He and Dr. Varmus are planning some different activities related to international health. They are both together in Durban, South Africa, this week, moving ahead with the malaria initiative. One of the things that I think everybody would like is not only to do some research on malaria and try to do some things

like find a vaccine, but also here, on site, to train black African scientists, physicians primarily, to do research on the disease that is killing most of the people in their country.

Hannaway: Another committee you were on—this is 1978 to 1983—was the NIH Coordinating Committee on Manpower. Would you like to tell us a little about this?

Kirschstein: Well, [for] the research training programs of NIH as a whole, under what was a new law in about 1974, the National Research Service Act—after the money had been impounded, they brought it back—it was required that the National Academy of Sciences do a study, first every year, then every two years, and then every four years--the report will be done momentarily for 1998; it is coming out in 1999—related to the research manpower needs in biomedicine. That was part of the condition under which the Congress put back the Research Training Program. They felt that when Mr. Nixon had impounded the funds, and they began to look into some of the practices of our universities, the medical schools in particular, in regard to who got postdoctoral or particular training. The postdoctoral M.D. training really was part of a glorified residency program in which you were called a research trainee. Maybe you did a little bit of research activity, but you spent most of your time the same way you would have if you were just a resident. It was not very wholesomely run. So the Academy would show that those things were happening. When Jim Wyngaarden came, and even before him, Don Fredrickson, I guess was still here then, they felt that there needed to be some coordination of the programs that were being handled here.

Don Fredrickson actually brought a woman here named Doris Merrick to try to coordinate the research training activities that all the institutes did. Of course, NIGMS had the predominant research training responsibility, and she asked me to join her in that. We did do some things that would allow us to coordinate things better. We developed the now-defunct, but for a while it looked pretty successful, what we called short-term training, where we gave grants to train medical students in the summer for periods of three months. You could divide the medical students with research training for four years in a row, three months apiece, and then that would count as one year of getting experience with work. I think the schools began to include their research training programs. They are probably not doing that now very forcefully because they are all worried about managed care and how managed care is going to influence the medical school as a whole. I would not call that one of the major committees that I served on. But somebody, in the height of zeal, probably put it on my CV and I did not take it off.

Harden: I want to shift to asking you some general questions about the 1970s, but I want to note beforehand, since we are discussing each of these individually, that in 1980 you received the Meritorious Executive Award. What was that for, if I may ask? For anything in particular, or for a body of work?

Kirschstein: I think it was for a body of work. The Senior Executive Service was set up under the Carter Administration with the idea that they were trying to enhance the quality of the highest management in the federal government. All the people who were in the position I was in, namely as a director of an institute or here in Building 1 and deputy director, were grandfathered into the Senior Executive

Service. We did not have to compete for those jobs. Thereafter, when a position opened, there were a set of criteria, and we set some of them up here ourselves for our medical and research positions and our administrative positions. But among the criteria was that there had to be a nationwide search [for certain positions] and a search committee more like what academic institutions do. There were incentives that were provided, such as the possibility of getting a yearly cash bonus if your performance was outstanding, and it sounded wonderful. Up to 35 or 40 percent of the force could get bonuses. They then limited it to 20 percent and it never got above that. On top of that, certain individuals would receive one of two presidential-rank awards. So this was a group of people who would be nominated by their agency, be reviewed by the agency, be reviewed by the department, their names sent forward to the Office of Personnel Management, and then, finally, they would be selected. For this one, they probably did the selection for the next one, which was called the distinguished executive award—probably someone in the White House did it. The meritorious was a \$10,000 cash award; the distinguished was \$20,000. They just upped those recently. The meritorious was awarded by the Secretary in a ceremony; the distinguished used to be awarded by the President. Ronald Reagan loved doing it.

Harden: Did he give you yours?

Kirschstein: Yes.

Harden: In 1985?

Kirschstein: He got the plaques mixed up, but he awarded it to me in 1985.

Hannaway: That was your distinguished executive rank.

Harden: Did you go to the White House to get that one?

Kirschstein: I went to the Old Executive Office Building, and that was a very funny story in 1985. In 1980, my mother was still living, and I was going to be going down to the Department to get the award, and Al said, "Well, I cannot be bothered. You take your mother." So my mother went and saw the ceremony, and she liked that. She died before the next one, so I was pleased I had done that. In 1985—my husband was in the commissioned corps, so he could not get anything like that—Al was going to go with me. We got down to the Old Executive Office Building and they cleared me through, and they could not find any clearance for him, although he had sent it. They kept telling me to move, and I said, "I am not going without him." I made them do the whole thing and get it, and finally he got cleared to go in with me.

Hannaway: You did not have your son with you?

Kirschstein: No. In 1985, he was, I think, interning at Boston. No. I do not know what he was doing, but he did not come. Each of those awards was lovely. But it is—I will toot the horn just a little bit—very unusual to receive them twice, and I did receive each one of those a second time.

Harden: Wow. I did not know that. I do not think that you put that on your CV.

Kirschstein: It may not be. I do not know. I think the [second] meritorious was in 1992 or 1993 and the [second] distinguished was in 1995 or 1996. That made me feel good.

Harden: Certainly.

Kirschstein: It is for a body of work, I think. In fact, they are said to be that. The cash awards,

the bonuses, are supposed to be for something you did that year that was particularly outstanding.

Harden: I want to generalize here for a moment and note that by the end of the 1970s, there was a lot of economic constraint at the NIH because of the inflation in the national economy. I wondered if you could describe the discussions that were going on among the institute directors about how to deal with that problem. You were successful in breeding more scientists, as it were, attracting more scientists into science, but the pie of the dollars was shrinking and you were having lots of criticisms about who was getting grants and so on. What were the conversations? How were you going to address this?

Kirschstein: The conversation was about the dysfunction of the system, about how one could make it function better, and how one could bring stability into the system. It became more enhanced [prevalent?] under Don Fredrickson's regime probably than before that, and Don came in 1973, something like that.

Hannaway: Seventy-five.

Kirschstein: Seventy-five. Stability began to be defined by the group who were discussing it, despite some misgivings on several people's parts, as the ability to award every year at least 5,000 new and competing research grants. That would give you a reasonable percentage of what at that time was being submitted, something on the order of a third. The problem was that very quickly in the eyes of the scientists, in the eyes of the congressmen who did the appropriations, and in the eyes of the OMB and the Administration, it was not at least 5,000 which would be a floor from which one could rise, but it became a ceiling that had to be met regardless of

the dollars appropriated. The only way that that could be done was by taking grants that asked for \$125,000, cutting them to \$90,000 or some much lesser amount of money, garnering that money and using it for other grants. This was the infamous downward negotiation which allowed nobody to do as much as they could do and really was something that many of us were deeply concerned about. Now, Don had all the good intentions in the world. All of us did. Several of us warned him. But it became—and he knew it, and he tried very hard—almost a mantra for many years and, in fact, remained a stain for a long time. Also, because of that, it shortened the period of time for an award, and then you lengthened it when there was more money. It was really a very bad time. And you could say philosophically that there were some very interesting arguments. If more young people can get into the system, we can move faster. But at what expense? If you cannot have enough money to do good research, will the research suffer? We sat for hours debating these things. There is no good answer under those circumstances. I suspect, in retrospect, that we had to do it. Probably the hue and cry would have been so great if we had not. I wish we had probably stopped it sooner. How much that accounted for Don deciding to leave when he left, I do not know. It is hard to tell.

Harden: That leads me into the next question I want to ask, which is one that we have added and that you do not have, and that is, would you go into a little more detail about Don Fredrickson as an administrator and compare him with Jim Wyngaarden. You have mentioned both of them, but can you give us a little more detail on each of them and how you, as an institute director, interacted with each

of them as well.

Kirschstein: I had known both of them. I knew Don as an intramural scientist first, and for a short period of time, when I was in the Division of Biologic Standards, just before or maybe the year before it transferred to the Food and Drug Administration and for a short period after it did, I actually represented the Division at the scientific directors' meetings. Don, of course, at that point was the scientific director of the Heart Institute. He had been the director for a while. He had gone back to being scientific director. So I knew Don fairly well. Jim Wyngaarden I did not know here. He was long gone before I would have known him. But he was involved with the Medical Scientist Training Program, first at Penn, then at Duke. He was on a number of NIH advisory groups. He chaired, I think, the group that looked at how the Division of Research Resources should be reorganized, and he was the one who wanted to put them back together, and we sort of developed a natural affinity for each other. Jim felt that he could not trust them, so he would talk to me. Don had other interests. When Don became director, the one thing that I worked with him on particularly was that he was interested in the recombinant DNA activities, and he set up the rack [?] and he held the public meetings. Since the recombinant DNA and rack [?] was in NIGMS for a period of time, we worked closely together. Both of them were not heavy-handed administrators at all. Don knew this place incredibly well. Except for his year at the IOM, he had basically spent his entire research career here.

Harden: Let me stop for a moment.

Kirschstein: Don had spent virtually his entire research career here at NIH, except for the year

when he went to the Institute of Medicine. Don had a very interesting tenure here. He sat over in that office, and there were many times when, instead of having an institute directors' meeting in room 151, he would decide he wanted to have them in his office. Were you ever in Don's office while he was director?

Harden: I have heard stories about it.

Kirschstein: Yes. Don was, and still is, married to Priscilla, who is from Amsterdam and who loves certain types of unusual furniture and unusual rugs. She likes to have a table at which one sits, maybe to eat—I was never at their house for dinner, though I understand she was a fabulous cook— either for a meeting or whatever, covered by a Persian rug; Persian rugs on the floor; overstuffed couches; and high, carved doll-like wooden chairs all around the office. The first time I ever saw this was when Marshall Nirenberg won the Nobel Prize, and Don was then either director or scientific director of the Heart Institute. I do not know which because he was both. They decided to have a ceremony in Masur auditorium to honor Marshall the day the prize was announced, and we all went over. Here on the stage was this enormous velour overstuffed, deep rosy purple, I guess, couch that Mrs. Fredrickson had insisted should be moved down so that Don and Marshall could sit on it during the ceremony. I had not seen the rest of it at that point, but I saw the couch. When Don moved in here [to the NIH Director's office], he brought the couch, he brought the Persian rugs, and he brought the little chairs. There were other chairs, too, but most of the chairs were little. There was enormous incentive on the part of the institute directors to get to the ICD directors' meeting early so they could sit on the regular chairs.

Harden: It was a brilliant stroke on his part, don't you think?

Kirschstein: No. I think it was Mrs. Fredrickson. Don was very nice. We got along beautifully. In the end, he took a lovely picture with all of us, and he was really quite sentimental. I think we were all sorry to see him go. We really were very, very fond of him. Jim Wyngaarden was next. I remember walking on the NIH campus with my husband on a beautiful sunny May, I think, and finding Ted Cooper, who had been the director of the Heart Institute before Don, and who became the Assistant Secretary for Health under Gerald Ford's administration, and lived on the campus. So here was Don walking a bicycle with a helmet, and Ted, who was maybe three inches taller than I am, which is very small, maybe a little more, walking beside him. Now, that was prior, I guess, to Jim Wyngaarden. I said to Al, "They're talking about the directorship," and it turned out that that was true.

Hannaway: Yes.

Kirschstein: Well, Jim and Don had been friends, and when Don decided to leave, I think he suggested Jim, and they accepted that. That was considerably later. It was in the Reagan-Bush era. Jim came, and I was one of the first people who talked to him. Now, at Duke, from what I have heard, Jim was a very strong leader and a very strong administrator. He had a lot of power in the department. Not always a strong administrator and that you can strike. But he had a lot of power, which accrued to department chairmen in those days. He came here and he accepted the job of director either not understanding, or maybe not wanting to understand originally, that the director of NIH does not have any money, and does not have a

budget. He said, “Ruth, what have I done? I cannot do anything here.” I spent a lot of time persuading him—I am not sure that I ever succeeded—of the importance of moral suasion, because Don Fredrickson was, in my view, one of the most powerful directors we ever had. What he did with the recombinant DNA, what he did with the stabilization, rightly, wrongly, or indifferently, he used his office and his moral suasive powers—he was a magnificent orator—to convince people that what he wanted to do was right. He also knew what in those days he should not ask for. There was a great deal of discussion about whether, with the budget being tight, regardless of whether it was or not, whether the director of NIH should have—which the director has now—a discretionary fund, some money put aside for certain projects that would be important. Don said, “No, I do not think I should. I think the money is so tight that I think it should all go to the institutes. I will work with them.” And through his suasive powers, they would do it. Jim Wyngaarden is very soft-spoken, and not a very good speaker in public, I am sure. Privately, he was fine, and, furthermore, if you are the chairman of medicine, if you say jump, they will jump. Whether you say it well or poorly, it does not really matter. Jim never quite learned how to do that and never felt totally comfortable, in my view. He did some very good things, and I would have to stop and think about them, but he did some very good things. He loved to travel, so he was out of here for a good bit of time. More than Don, he would delegate, so that when he was gone, Bill Raub, who was his deputy, really was able to take charge of the place, and continue to move things along. Jim did one very important thing, as I think about it now. Marvin Cassman, who

is now the director of NIGMS and who was my deputy director, and I realized in the 1980s, probably around 1985, 1986, something like that, that the next big important scientific endeavor after recombinant DNA was going to be the importance of physical-chemical things like X-ray crystallography and NMR to have an effect on medical formation, the development of drugs, and so forth. As the AIDS epidemic was raging and there was this intramural push to do AIDS research that was when Jim finally got some money, \$10 million. You could distribute it the way you wanted to within the intramural program, and I said, “Look, it’s a great achievement. Nobody else had that before.” We persuaded Jim to go with us to the Academy to hear some of the real mavens on X-ray crystallography, and he listened and realized it. Jim turned both that program and especially NIGMS’s program very heavily toward X-ray crystallography and gave us some extra money for it and gave that to the program. It paid off. The retroviral, anti-retroviral drugs some of the work on AZT, is very important, and he did that.

Harden: He was here. Also, it was still a very tight economic situation.

Kirschstein: Yes.

Harden: I interviewed him when he left, and at that time, he was thinking along the lines that he saw his role as director as not letting the place slip backwards—not that he could go forward very much.

Kirschstein: Exactly.

Harden: Would you agree with that?

Kirschstein: Yes, I would agree with that. That was why he originally was very much against

NIH having any role in sequencing the human genome. He did not feel that, with money as tight as it was, that he could afford to spend any NIH money on that. Now, the scientists out there were convinced that it had to be done by NIH. The Department of Energy was also working on this. Jim sent me all over the country [on missions] related to genome work. I went up to Cold Spring Harbor. If Jim was going to do it at all, it was going to be a tiny little bit of the NIGMS program which had genetics. I went to a Cold Spring Harbor meeting—no, I am sorry—a Woods Hole meeting of the Academy. Senator Pete Domenici, who represents New Mexico--they were doing most of the genome work out at the Los Alamos National Laboratory and wanted to be sure that they kept their activities-- held a hearing out there, and people importuned Jim to go and stake out NIH. You cannot let the Department of Energy beat you to it. And Jim would not listen, but he sent me out there. The result was that once afterwards, in a hearing downtown, the Senator said, “Oh, that’s the little lady who taught me all about genomics, told me what the genome was about.” Then, finally, a person who had been a mathematical scientist here at NIH, Charles DeLisi, was made the director of energy research at DOE. He had a very minor job here. And he began to say, “We’re going to beat NIH out in doing the human genome,” and Jim could not stand that. That was when he said, “Okay, Ruth, start the program moving.” Then the community rose up and said, “We cannot let a government bureaucrat, particularly a woman, run this”—I told you the Jim Watson story—and so they got Jim Watson and moved the program out.

Hannaway: That had certain consequences, too.

Kirschstein: That had lots of consequences. Yes, some very interesting consequences.

Harden: Before we move finally to the 1980s—and I say this because AIDS became such a big portion of the focus for NIH—can you recall discussions---

Kirschstein: Of what?

Harden: Of NIH's concerns, let us say. I do not mean research entirely except for NIAID perhaps. But can you recall discussions in the late 1970s, before anybody had any idea there would be an AIDS epidemic, about which direction people saw research going? Did they see, aside from AIDS, where things were going, or were there other surprises in the 1980s and later?

Kirschstein: There were lots of surprises in the 1980s, I think. I think most people felt that there would be the molecular genetics revolution in the biotechnology and that it would get larger and larger, and it did. I think there was much more emphasis, for a while in the 1970s, in the Cancer Institute particularly, on chemotherapeutic drug testing.

Harden: Yes.

Kirschstein: There was a lot of clinical activity in the other institutes, and basic science only came into its own later, in the late 1970s, which is to say NIGMS. But there was not a lot of planning. There was full confidence that we could probably support research scientists out there. Their ideas were wonderful. There was need, in many people's view, for research training, and Jim was a strong component of that. Particularly, he was concerned about improving how post-M.D.s and M.D.s were trained for research and he knew that his colleagues—he probably had himself—were misusing the funds. I do not say that in a way that says they were

crooks, but they were not really using them to teach.

Hannaway: They were applying them for their own purposes.

Kirschstein: They were applying them for their own purposes, yes.

Harden: Was there any jealousy among the institutes because of the fact that Cancer had received so much money?

Kirschstein: Oh, it was terrible. The 1970s was the worst period, and a little bit of the early 1980s. Now, I cannot tell you what it was like before I became a director. I was in the Division of Biologic Standards, and then I was out at the FDA. Although I did a number of things here—I did some contracts and I ran a committee for Leon and some other people—I really do not know. But clearly, the institutes were fiefdoms. Now they are states where they were union, I think. Then they were fiefdoms. And Jim was correct. They had enormous power unto themselves and enormous autonomy. I remember, because I am a very outgoing person and I believe in collegiality, trying to develop some things. Actually, Don Tower, who was the director of what was then the National Institute for Neurologic Diseases and Blindness, sort of felt the same way I did. And he said, “Why shouldn’t we institute directors talk to each other?” Jim Wyngaarden was not a very good communicator, and one of the things that happened early on was that a couple of institute directors—and Fredrickson too—a couple of institute directors—and, of course, Jim was in the 1980s, so I am getting them a little mixed up, but nevertheless—would be told some things about budget in particular at an ICD directors’ meeting which were still confidential, the President’s budget was not out, etc. Realizing that they were going to suffer, their institutes were going to

suffer, the story got out very quickly. When that happens two or three times the director stops talking to the institute directors about the budget. So we had very little dialogue at certain times in the 1970s, in the early 1980s some too. And Don Tower and I said, “We ought to talk to each other.” The problems were mutual. “Let’s have a brown-bag luncheon once a month.” The first time we had one, nobody came. So I said, “Well, I’ll tell you what. I will buy cookies if you will come.” So I used to be known as the cookie lady. They did come for a while. Then they stopped coming. They really wanted to work by themselves. They really were autonomous. There was enormous jealousy, not only between Cancer, but the bigger ones—Heart. Bob Levy was here as the director of the Heart Institute, and everybody knew that Bob had a special relationship with Don Fredrickson. Bob described it as love-hate. I am not sure everybody else realized that, but I did. But, anyway, it was not a time of collegiality.

Harden: And you think that has changed significantly.

Kirschstein: It has changed enormously under Harold. You know, Don was a great scientist. Jim Wyngaarden was a great scientist. They both were elected to the National Academy of Sciences at an early age. Bob Stone, Bernadine, we will leave out for now. We have never had, since Shannon, a director of such intellectual capacity. The stature of a Nobel laureate who has, beyond anybody’s wildest expectations, and in fact beyond any expectations, because the one thing that I think everybody was concerned about was would he really want to manage this place. Harold saw immediately that the mode for the 1990s was the fact that scientific disciplines were intertwining and that the institutes had to become

collegial and that he was going to make it happen, and he has. Absolutely amazing. I do not know, but I do not think we will ever go back. The Nobel Prize helps his ability to see the picture clearly and yet take care of the details. I think I have told you, haven't I, that our crackerjack budget team downstairs comes up here to present the budget, and Harold looks at the spreadsheet and says, "That number is wrong." Now, he cannot do the mathematics. It is true, he cannot. But he can do approximate percentages very rapidly and say, "That cannot be right." Inevitably what has happened is that with the computers that they use now, unless they actively make sure they have a spreadsheet and they go through on the numbers which were there before under a different circumstance, unless they check everyone to make sure, sometimes the old number creeps in and they cannot find it. He sees it right away and many things like that. Of course, he has had the opportunity, and used it so wisely, that no other director has had of appointing this vast number—it must be nine now, and maybe it is more than that; I really have not counted recently; the last time I talked about it, it was seven, but it is more than that now—of new directors of institutes who he chooses regardless of their management abilities or their science.

Harden: I am going to follow up on this. We are jumping a little ahead, but can people be the director of various institutes and the director of NIH and continue doing the same level of good science?

Kirschstein: Not the same level. But if they are willing to cut back, they can. Harold does.

Harden: I know he does. Kirschstein: He is doing it remarkably well. He is spending more time in the lab now than he did the first few years he was here, because he is

more comfortable with what he does here now.

Hannaway: He was learning more at first about how the place works when you are actually here.

Kirschstein: Yes. But what he knew right from the beginning, when he came, was, back in San Francisco, he had probably a lab of at least 20 people. He _____ six and he's kept it to about that level. He gets scads of requests to come to work with him as a postdoc—he's always gotten them since '89—and now he's extremely selective and only picks a very few to be a manageable size. He told a friend of mine, whose daughter is a very bright college student and wanted to come work for him, even on a volunteer basis for the summer, that he would not take her because he believes that when you take a student who's never worked in the lab before, you have an obligation to mentor that student intensively, and he did not have the time to do that. He takes scientific mentoring extraordinarily seriously, and he's changed this entire campus in terms of how mentoring is to be done. I wouldn't guarantee that every scientist is doing it, but it is becoming part of their reviews.

Harden: He's the first director since Henry Sebrell to have a lab at the same time he's director. Jim Shannon apparently thought it had to be separated.

Kirschstein: Yes. Shannon thought it had to be separated because Shannon came to this job having been the director of the Heart Institute, but also came when he had a crisis. Shannon became the director, we said, because of the Cutter incident, and there was a real threat to whether NIH would survive. I mean, you know, you were responsible for something that you shouldn't have done, and he had to put the place together again, and he did. And he also believed that they should be

separate. Harold does not.

Harden: Do you think it's just individual style? I mean, Shannon functioned this way and... I'm looking at the two—

Kirschstein: Yeah, I think it's individual style. I think Shannon, after he was young, when he was at NYU, never worked at a university again. He went to Goldwater Memorial Hospital, but he went there under the aegis of World War II work on malaria. It was a directed program. And he went from there to Squibb and from Squibb to the Heart Institute. Harold never worked anywhere but a university, where the dean gets selected and has to have tenure in a department or they won't choose him as a dean. So it's partly background, partly style, partly values. And Shannon was building a very small NIH into a big NIH. Harold is not building it. He, I know, would prefer not to have new institutes. I know, regardless of the fact that it's complementary and alternative medicine, even if it was anything else, I do not think he wants a new institute or center or whatever you want to call it. He wants to improve those that are here and make sure that science is covered.

Harden: Now I'm going to ask you a flippant question. As we're going to have stop soon, I think, for this round, I have observed over the period of time that he's been here that he is wearing a tie much more often than he did when he first came. What does this mean?

Kirschstein: He decided early on that he was not going to wear a tie to work in this environment unless we had dignitaries coming. Or if he went to Congress, he soon found out that he was expected to put one on when he went to Secretary's meetings or other places like that. He has a little room there where he keeps a set

of appropriate shoes and clothes and so forth. We sit in full staff meetings on Friday mornings when the weather is good, even if it's very cold, and he will have biked out. Now, I do not know much about biking, but I have been told that even in the coldest weather, if you bike as many miles as he does, you are hot and steamy when you get here and you cannot peel those clothes off and get into a shower and get into different clothes without a cooling-off period. Well, if he gets here at 9 and the staff meeting is scheduled for 9, we sit with him in those clothes, and it doesn't bother him. And if he has to see an institute director in those clothes, he will. He has figured out where he should wear them and where he shouldn't. He went to—well, he met the other day with some outsiders and decided it wasn't a tie time, so he did not wear a tie. He wouldn't sit with them in bicycle clothes, I do not think. He met with the German minister of health without a tie. [Turn that off.] But the enormous success of the NIH in terms of its budget in Congress and everywhere else at a time when the Education Department is suffering, and most of our fellow agencies within HHS are suffering, we are not the darlings of anybody but Donna Shalala down there. I need to think of what may happen in _____. I spent a lot of time down there cooperating with those people, accepting things they want me to do, talking to them, being nice, understanding their problems, and he's _____ to do a little more of that. Shalala has a meeting, a luncheon meeting, which he never bothered to go to, and he's been going faithfully for _____ recently. So I think he knows.

Harden: Very good. Well, I'm going to stop here today, if that's all right, and say thank you.