

Interview with Dr. James B. Wyngaarden at the National Institutes of Health.
July 25, 1989. Interviewer: Victoria Harden, Ph.D.

Harden: Dr. Wyngaarden, would you begin this interview by describing for us the home in which you grew up and tell us a bit about your parents, your grandparents, your siblings, what did you enjoy doing as a boy, and talk about your elementary and secondary education?

Wyngaarden: I was born in East Grand Rapids, Michigan. I lived in Grand Rapids, just across the border, and lived essentially all my life in one house. My father was a theological professor at Calvin Seminary in Grand Rapids and my mother was essentially a homemaker although she had a fairly rich background in music and in art, primarily painting. She continued to do some of that, although not when the children were young. She took up painting again after my father retired. But there was that kind of a cultural tone, a considerable emphasis on scholarship and learning in the house. Not oppressively so, however. My father had about four advanced degrees. He had a Ph.D. in Semitic languages from the University of Pennsylvania and then additional work at Princeton and Yale before he assumed a position there. And so it was just the cultural tone of the house. There were lots of books. We were reading a good deal. I read a good deal. We didn't have the distraction of television, and we didn't use the radio much. I used to listen to some sporting events and to the evening news. Otherwise, the radio was not on during the day. It was just that my

parents didn't have it on. It wasn't that we weren't supposed to listen; it wasn't the custom. We spent our time doing what normal kids did. We played a lot. I was really quite athletic, and for many years my father used to worry about whether I was going to become serious about anything. Athletics seemed to dominate my mind. I was a fair athlete in local competition. I was ranked number one in tennis in the city in my age group. I was an all-conference high school basketball player and that sort of thing, which at the time was terribly important. Much more important than anything else. But I was also a good student. I graduated at about the top of my class in high school. Things went along in a pretty casual manner. We spent summers at my mother's relatives in Iowa. She was from a farm family, and my grandfather had done very well in farming and had quite a lot of land. All the children had farms when they grew up, and when I was very young, I thought that was the best life in the world. I used to dream about being an Iowa farmer. I spent summers working there when I was ten, eleven, twelve years old. By the time I was thirteen, I discovered it was really hard work, and I got more interested in high school in other things and really have not been back much since then. But that was an important influence, too.

I went to what was called a Christian grade school. It was not exactly denominationally-owned, but it might as well have been. It was the equivalent of the Catholic school system except that it was a Protestant denomination. Then I went to Grand Rapids Christian High School. It

was a continuation of the same program. It was a society-owned school but there was a strong religious emphasis--chapel every day, for example. That kind of influence couldn't help but have a considerable influence on my sense of what is important in life, and, of course, on my ethical approaches to many of the kinds of problems we've encountered here. We can come back to that later. But I would say that I was no different from the other kids in the neighborhood or the school except that I found studies interesting and that I read a lot. But my primary interest in those early days was athletics.

Harden: I can already guess the answer to my next question. Who were your boyhood heroes were and why?

Wyngaarden: I suppose I would have to say that early on I was most impressed with sports figures. Hank Greenberg and Lou Gehrig and pitchers like Carl Hubbel and Schoolboy Rowe. Those were the great names from my early days. Beyond that, I used to read a lot of biographies and I didn't know personally great and famous people but I was very impressed when the President came to Grand Rapids to campaign. That was Franklin Delano Roosevelt, and the first opposing candidate I can remember was Alf Landon--both of whom came in the same year. That gets me back into 1936, I think. But I can't really single out any particular person. I used to read about in school. But I used to read about early church leaders like Savonarola, Martin Luther, John Calvin, people like that. I used to have to do papers on people like that so I tended to learn a lot about them.

Harden: When did you make the switch into considering medicine as a career?
What caused you to do this?

Wyngaarden: I've been asked that before, and I can't cite any special event. I was always interested in science, and in high school I took all the science and math courses available. I worked a couple of summers in a local hospital in the emergency room. I primarily assisted with holding limbs when plaster casts were put on, and that sort of thing. In college I considered myself a pre-med student, although college went by very fast and I found myself in medical school rather quickly. I graduated from high school in February 1943. We were in the war. I had accumulated some advanced credits from high school, so I started college locally in the fall of 1942. I had overlapping semesters and then one full term of college. Then I went into the Navy program and was assigned to Western Michigan College of Education, as it was then called. Now it's Western Michigan University in Kalamazoo. This was a school without a lofty academic reputation, and yet I discovered that I received a first-rate education there. I learned something very early: someone who wants a good education can get it in many, many places. You don't have to go to Harvard or Yale. There are many other choices, and Western Michigan was no exception. There were some superb teachers there. They had the strength of the faculty because there were about 1600--mainly recruits--in this program. We went to school continuously. I had three terms in one twelve-month period. I had accumulated 96 hours, and so I was admitted to medical school in the

Navy program. It wasn't to start until October of 1944, so I was assigned to a hospital in Davidsville, Rhode Island--a Seabee base hospital--Camp Endicott--Davidsville, Rhode Island. I spent the summer there--about four months. I started out without much of an assignment, but the person who was running the chemistry in the laboratory went AWOL, and the Director of the lab asked me if I had any particular interest in running the chemistry department. So, I did. I had enjoyed organic chemistry and other in college but I didn't have an extensive chemical background. I ran the laboratory for about the last three months. And that was very good experience. I ran the chemistry but I didn't do blood work. In October, I was transferred to Michigan, Ann Arbor, and entered medical school in the class of 1944. We were on an accelerated program in medical school also. We were going continuously with a week's break between terms. No summer vacation. We finished about three terms when the war ended--in the spring of '45. It was in May of '45. We had --something's wrong with that chronology. Those years were right. We had been on this accelerated program and we stayed on it for a time and then decelerated and we had fairly long breaks in order to get back and register with the original schedule. The class ahead of us was past the midpoint and they stayed on the accelerated schedule and finished early. We ended up being the top class for two years, because when we were junior medical students, there were no seniors. This was in a way an advantage because we got to do more than we might otherwise have done. But we also had these

breaks in continuity. Long break initially and then a summer vacation. It was probably three months--four months time. I spent that time in the pharmacology laboratory. It was the most exciting, the most dynamic of the Michigan science departments at that time. I had a really good experience there and published a number of papers from that experience.

Harden: You were interested in research in medical school.

Wyngaarden: Yes.

Harden: And was it this experience or this and others that piqued your interest in research?

Wyngaarden: I suppose I could have been turned off. But I had already had that interest. In fact, in the Navy program at Western Michigan there was also an opportunity to go on in some other fields--it was in the Navy in engineering and dentistry but nothing in chemistry. Had there been, I might have been tempted to do that. But I went into the medical program and when I got into medical school, I progressively found that one could combine chemical and medical interests which is what I always hoped to do and I continued to do that and when I finished medical school I was fortunate to be appointed an intern at Massachusetts General Hospital and there they had had a practice before the War of staggering appointments. I think everybody started in July. At least, by my time they all started in July but some of them had a second year that began the following July. Some of them were off in the summer and started in September and then the third year--the residency year--some started in July and some started in

September and some in January. So, there was sort of on a staggered appointment and I happened to have two consecutive years and then six months free and I made arrangements to work in the thyroid laboratory during that time and did. And again, it was a growing laboratory and it was fairly chemical in some of its influences. We were studying how thyroxin was synthesized in the salt-free system. I didn't have any experience that would qualified me to do that but I just picked up the journals and studied the procedures and started. And we actually made some interesting discoveries in that year. One of them had to deal with a series of monovalent anions and I had discovered in my readings discovered a fast cyanate had an effect on iodine uptake in the thyroid and it would flush out a certain amount of unbound iodine in the thyroid as well. And I knew from some of my reading that I had done that summer in Rhode Island that I had undertaken to repair what I thought were serious deficits in my college education. I had taken up physical chemistry, for example, so I read a text in physical chemistry in my spare evenings and I had a lot of free time. I had recalled the Hoffmeister series which was a series of myocrylic anions with some ranking of affinity for binding with albumin, as I recall it. Paracyanate was one of those and a number of others were also--perchlorate. Similar monovalent anions I thought it would be interesting to see if they would have a paracyanate so I could track down the thyroid. And it turns out that they all did. And the most powerful of these ions was perchlorate. So, we did some additional

work with that. For a time it was used in therapy for a child with hypothyroidism. It didn't turn out to be the safest drug for that purpose. But now it's used as a diagnostic test. There's a perchlorate test that is applied; that is, perchlorate is given to someone after radioiodine. The dose and the amount of the perchlorate that is washed out of the thyroid is an index of the failure to bind the iodine that has been taken up. That was a clue to certain thyroid disorders. So, it has proved useful. And other people that had picked up that discovery and worked on other ions. In fact, Leon Wolff here at the NIH has done quite a lot of work in that area years ago and it was discovered that the critical feature was not only the charge--the monovalent charge--but the hydrated ionic volume of those molecules and that actually led eventually to the discovery of pertechnacetate which is the standard compound used in diagnostic work in thyroid physiology. So, from that one summer's work quite a lot came of it. Although I didn't personally because of later involvement. I might continue with the influence of that experience at the Massachusetts General Hospital. We made a call in 1951, I believe it was, the Korean War broke out and I had in my earlier experience in the Navy had considerable education by virtue of support by the Navy or actually assignment by the Navy and those of us who had had such educational experience is owed two years of service as a repayment, as it were. Since the War ended--the First World War ended--we were never required to do that, although I had credit for some time and that was later in Boston in the

reserves. But having had less than two years of active duty service at the completion of my educational experience, I was eligible for service in the Korean War and would probably have gone in the Army except that Jim Shannon came to Boston. So, he at that time, had rather recently come to the Heart Institute from Squibb and his position was Associate Director in charge of research in the National Heart Institute. At that time it wasn't called Heart, Lung, and Blood. And he had during the War, led the malaria research project at Goldwater Hospital in New York and in order to conduct those studies he had brought in some young residents from the New York schools to take care of the patients that the scientists would be studying. As a matter of fact one of those young residents was Bob Berliner who later was very well known here. When Jim Shannon came to the Heart Institute and he realized the Clinical Center was about to open, in fact, I'm sure that's one of the attractions that brought him here, he set out to recruit eight residents with strong research interests to come to the Heart Institute and be here when the Clinical Center opened. But also to engage in research. And he visited just a handful of leading institutions at that time that included Johns Hopkins, Washington University in St. Louis, Cornell and Columbia in New York and Peter Bent Brigham and Massachusetts General and Boston City hospitals of the Harvard system. And maybe others but those I know he did. And I met with him in Dr. Walter Bowers' office, Chief of Medicine's office. I had never heard of the National Institutes of Health at that time. And I talked

with him and he offered me a position in the Heart Institute. And there were eight of us selected; Don Frederickson was also one of those eight. He was at the time at the Peter Bent Brigham Hospital and I was at Mass. General. So, we were in that same class and both later Directors of the National Institutes of Health.

Harden: Dr. Wyngaarden, I'd like to come back and ask you one more question before we move on a bit chronologically. You have clearly shown that you've had a great affinity for research from medical school. Did you ever consider private practice as an option?

Wyngaarden: I don't think I ever seriously considered community private practice as an option. I was interested in academic medicine from the start. And I had fairly to complete clinical training at Mass General Hospital. And later when I got to the NIH, the studies I did here and at Duke were heavily biochemical and for the most part laboratory-based, animal tissue type studies. They'd include from time to time forays into clinical research when I thought there was something worth testing in human beings. But I never really viewed myself as a community practitioner. In fact, I think that was solidified in the last years of medical school when, as I indicated, we were as a class given more responsibility because there was no senior class during our junior year. And there were some extended assignments on clinical services when I thought we were really not learning in the sense of acquiring information, obviously, we were developing skills and healing sick people, but there were some of those assignments of newborn

pediatrics, for example, in which there wasn't much interaction with patients. It was parents, mothers, in particular. And the other experience that I found that probably solidified is an assignment in obstetrics in a community hospital. And we would sit and stare for hours on end just waiting for a delivery to occur. And I found that just *so* painful. All that good time being put to no good use. So, I discovered quickly I could come in the morning and discovered that my classmates had already signed up for whatever deliveries there were and I went off to the pharmacology laboratory and I'd check in occasionally and once in a while have to come back and see if something was going on. We were so poorly supervised nobody knew, so I got an extra month of research out of that. And the exam was strictly from the book, anyway. So, I discovered from these exploratory experiences in medical school that I really was much more stimulated by problems that I had a very high level of intellectual investment. I was much less interested in procedure-based specialties. And quickly ruled that out. I never seriously considered surgery, for example.

Harden: Well, now, let's go back to where we were. You had just been recruited by Jim Shannon for the Heart Institute. But I know you made a detour by the Public Health Research Institute in New York. Would you tell me about that?

Wyngaarden: Well, at the time we were recruited the Clinical Center was not yet opened. It actually was, I gather, delayed a little bit, although it opened in

July of '53, I think. And I had some intervening time. I was about to finish my residency in the Public Health Service; it was probably about seven or eight months after I entered. And during that time, I was invited twice to come to Bethesda to visit the NIH here and in Baltimore because some of the Heart Institute group is still there at the Baltimore Marine Hospital. Luther Terry was head of that unit at the time. He later became Surgeon General, as you know. Bob Grant was there and several other young cardiologists. So, I visited there; I visited here. The group I primarily visited was Sidney Udenfried, a group which was very biochemical, which was the direction I thought I wanted to go. And then I talked with Shannon. And I had an intervening year, as it turns out, to finish in Boston before the anticipated Clinical Center would open here. And I was interested in this interface between chemistry and medicine and particularly in medical diseases and hereditary diseases. We talked about three laboratories. I visited two. One was Carl Corey's in St. Louis; another was Jack Buchanan's. At that time, he was at the University of Pennsylvania. And the third was Hans Stetten's--DeWitt Stetten's--laboratory in New York. I didn't know much about Corey and Buchanan. They would have been good choices, also. But, Stetten's name I *did* know because he had been at Harvard and he had worked with the group at this Peter Bent Brigham Hospital. I did not know him personally. But his fame preceded him. He was known as a spectacular teacher. Which, indeed, he was and is. And he was working at that interface between

biochemistry and medicine. At least, some of his studies were related to the metabolic defect of gout, and multiple diseases and so on. And so, I went to visit Buchanan and Stetten. And either assignment would have been fine but I listed the Stetten laboratory as my first choice. And Shannon worked that out and I worked there for a year. So, I went there in July of '52. I'm sorry, January of '52 and stayed until about February of '53 when I came here.

Harden: I was talking to Hans Stetten myself in preparation for this. And he impressed you but you, obviously, impressed him. He told me he went home and told Marjorie he thought he had just talked with the future Dean of Harvard Medical School. And it speaks very well.

Wyngaarden: Well, that's very flattering but the one thing I've never aspired to be is a Dean. (Laugh)

Harden: I would like for you to talk a little about this research you did with Dr. Stetten there and then later at the NIH, you know, when you were in the Arthritis Institute and the Heart Institute as a young researcher. The kinds of things you could do and couldn't do and perhaps reflecting on how it is now for young researchers.

Wyngaarden: When I was in medical school in the Navy, we also had a chance to buy textbooks and they would pay for them. And I bought one book which was called *The Basis of Metabolism*. And in it was a chapter on gout written by Walter Bower [sp?] and Cowey Manclammerer[sp?], who was a biochemist. And I was very much influenced by that chapter. As I

indicated, I was very much interested in chemistry and its interface with medicine. And here was a particular disease in which there was a substantial amount of chemical knowledge about uric acid, purine, and its relationship to nucleic acid and so on. And so, when I visited Stetten's laboratory in New York, and discovered that he was working on this problem of the metabolic defect of gout--that was one of the attractions of going there--I actually ended up spending a lot of my research career on the problems of purine metabolism and later got involved in additional studies of the metabolic defect in gout and far beyond that in the whole issue of how urine is synthesized and how these are regulated. And when at Duke, after leaving the NIH, found that the defect--the end product control mechanism which had been described in bacterial systems also worked in avian and rat systems. At that time that was the first demonstration of the universality of that controlled concept. There was, I suppose, no great surprise that the system applied to mammalian enzyme systems as well, but there had been no demonstration of that--just the bacterial demonstration. Of course, there were a lot of things that took place in bacteria that really didn't take place in the same manner in mammalian systems. It was at a time when there was so little information of that so that it created a bit of a stir and it was probably one of my better pieces of work.

Harden:

In doing this early work, I understand in one experiment, of course, you tested out your hypothesis on yourself and this probably would not be

permitted today. I don't know that that's true.

Wyngaarden: It wasn't really difficult. What I did was to synthesize label uric acid and took a substantial slug of this intravenously and studied the degradation of uric acid in myself.

Harden: What I'm thinking of here is your freedom as a young researcher to more or less do it all yourself and write it. In the climate today, do you think the young people have the same kinds of --

Wyngaarden: No. There's considerably more regulation. You know, I did the same thing with the perchlorate experiment. At that time, I looked up a lot of information on toxicity and there was quite a lot of it in the old German literature. About compounds. But I was just planning to give this to a certain number of patients and I thought before I did that I should take it myself first. I felt nothing from it. (Laugh)

It was really kind of foolish, but at any rate. Nowadays, that would be found out. All of these preliminary experiments in human beings have to be described, proposed to appropriate review committees at the institutions, and only after a series of approvals, is the scientist permitted to go forward.

Harden: Before you come to NIH as Director, you have a long period at Duke, at Philadelphia, what have you, in academic medicine. For our purposes in looking from the NIH point of view, how did you view NIH speaking as a person in the academic community, is what I'm trying to get at. Could you comment on this.

Wyngaarden: I came to the NIH in February of '53 and I stayed until about August of '56. And then I went to Duke from here. And before I left here I had a number of talks with Ralph Knutti who was in the extramural program in the Arthritis Institute, because I knew I wanted to continue some of these purine studies when I got to Duke. And he gave me some good advice as to how to structure a grant application and how much it was reasonable to ask for and those sorts of things. And so I had that application ready to go the minute I arrived at Duke. And it was funded and so I had my first grant early on. It was not difficult to get such funds at that time and I was supported continuously I guess for twenty some years, maybe longer than that. In fact, that grant still exists. It changes its title and eventually different principal investigators were named and I think at present Edward Holmes at Duke still has it. And it has been running since about 1956.

Harden: As an administrator at Duke, also, was there a feeling while you were there that there were good relations between the academic community and the government.

Wyngaarden: Oh, there's no question. The arrival of the NIH on the scene transformed American medical schools. Not only did I have a personal research grant but later I had a second from the Cancer Institute and I had a training grant. We had construction grants to build buildings with matching funds. There were career development awards. I had a career award from the Arthritis Institute at one time. There were career development awards. At

one stage when I was chairman of medicine, every division chief in the Department of Medicine had a career development award from the NIH. And, without the input of NIH money, the medical schools would have been the kind that I attended at Michigan in the '40s. A little bit of research going on. Very spotty. An occasional person would have substantial funds from some donor, would have an active laboratory to the envy of others. But, Michigan, which was far more research-oriented than the average medical school, was still a primitive place for research by comparison with the department at Duke when I was there and certainly more so, now. Now all of that was brought about by the NIH. There was some additional foundation money but prior to the advent of the NIH, most medical research was foundation-supported--Rockefeller, for example. And they became very minor players after that in terms of the quantity of money being made available. They were not minor, however, in the overall scheme of things because there's more freedom with foundation money. They're frequently willing to support risky ventures or innovative ideas on a pilot basis to catalyze new developments which you probably could not do with federal money. And if it is a good idea and comes along well, it may qualify for federal support the second round. But it's *important* money. Quantitatively, it would never had done to the medical schools what the NIH funds did. They have transformed education and certainly made the medical schools major players in life sciences.

Harden: One more question before we get you to NIH as Director chronologically. From my research it appears that this federal largesse in medical research sort of peaks around 1968 and then settles down and then in the '70s the training grants were cut. How does this affect you in the academic scene? Did you see this becoming a greater problem and its impact on bringing people up.

Wyngaarden: Well, the period from 1955 to 1968 when Jim Shannon was Director of the NIH was *clearly* the growth period. When funds were being made available in prodigious amounts compared with the Press Club. One year I think NIH supported something over 90 percent of all Study Section approved awards. And there were new programs for training; new programs for career development; there were funds for science construction. And those did peak at about 1968. If you look at the growth of the budget, it begins to level off at that point. Not exactly level, but it continued to grow but not at the same rate. And the investments of those early years have paid off in terms of training and more people. At about the time the budget was starting to level off or at least it assumed a much lower slow growth. These people were trained but not mature enough to start applying for those funds. Then the competition greatly increased. And, particularly, in the '70s. That's when it really became apparent. And, in spite of that, the NIH budget has continued to grow. There's been an overall growth rate of 2 or 3% per year and in the last seven years, it been better than that. But I don't think we'll ever see as flush with money-

-relatively flush with money--as we were in the '50s and early '60s.

Harden: A lucky generation. Now, we were discussing the constriction of the NIH budget. It slowed in growth and as the '80s began, 1981 or so, Don Frederickson left and NIH was looking for a new Director and you were invited to do this, and, as I understand it, from other people we've talked with, you really didn't want it to start with and I'm sure it must have been an awful challenge in a number of ways to presiding over this kind of thing. Tell me the story. Why did you finally decide to accept it? How did it go?

Wyngaarden: Well, I had had a lot of contracts with the NIH over the years on advisory committees and special review committees, for example; the Board of Scientific Counselors. I had served on the President's Science Advisory Committee, for example, in early 1970s, then on the President's Science Medal of Honor Selection Committee and I had been on a number of OSTP committees. I've had really a fair amount of experience in Washington. I testified largely through the invitation of the AAMC and the NIH budget a number of times. And as we've already discussed, most of my personal scientific training and accomplishments relate to NIH, of course. The successive departments that I chaired at Pennsylvania and at Duke largely depended on--at least for the research productivity--on NIH support. And so, I had the sense of the essentiality of the NIH in the scheme of things, particularly in that phase of medicine that I was personally interested in and identified with so closely. So, on the one

hand, I had the sense of obligation to at least consider this opportunity for me to do it. On the other, I was still enjoying the Chairman of the Department of Medicine role after 17 years. There wasn't quite the same novelty as in the early years. But, I hadn't really considered leaving Duke and when Ed Brandt first called about this, I really didn't think that was for me. There was another track of events going on at the same time and it was the Veterans' Administration. The first Administrator appointed for the Veterans' Administration was a man named Nimmo. And he was in the news a lot because he didn't seem to be giving his job much attention. He was off playing golf and he had also proposed passage of measures which would eliminate severely the research budget of the VA. He was in hot water because his wife was using the limousine to do her shopping and to go to the beauty parlor and things of that sort. So, he was in the paper and he stood out of those early appointments in the Reagan Administration as the paradigm of what we did *not* want at the NIH and there was a great deal of fear that we would have a Nimmo-type appointment, although it is exaggerated apprehension, a position like Mrs. Reagan. And when Ed Brandt first called it wasn't an offer. I mean, it was "Are you interested in being considered by the Search Committee"? And I said I didn't think so. Later he called again and we chatted a little more and I knew him just slightly. And he said would I at least be willing to send in a CV. And, I thought, "There's no harm in that. I'll do that. Probably won't lead anywhere anyway." So, I sent in the CV and I did realize at the time that

under the federal regulations of the Committee Management advertisement of filling out vacant positions that the applicant must apply and a minimal application is sending in your CV. (Laugh). So, I had met the minimal criteria by doing that. And sometime later there were short squibs in *The New York Times* and elsewhere of the list of candidates. And at one time there were about 12 or 15 names and mine was one it; then there were six names and then there were four names. So, and then I was asked to come up for an interview. And, it turned out in the end they submitted two names to the Department and to the White House and the two of us were interviewed and eventually I was offered the position. During that phase from sending in my CV until the request that I actually accept this position, a lot of my friends commented to me, "You *have* to do this; you simply have to do it. That job requires someone with your kind of experience who knows science, who knows medicine; has had experience with the NIH; knows a little bit about government; and someone who would bring credibility to the position." That was the term used most often: credibility to the position. You have to have someone in this position who has by virtue of his or her own background, the kind of credentials that speak to and speak for the scientific community. A lot of this job is representational. And, particularly with respect to the Congress. And, there was a great sense of relief. I think all the names that surfaced would have been highly creditable people but there was a great sense of relief when there was a genuine search conducted, and one which brought

forward names of people who, I think, --all of whom could have filled this position well. Not a single Nimmo type. And that was an enormous sense of relief. And, I think the same thing is happening right now. The Search Committee is just going about this in exactly the same way. The White House has given them the freedom to conduct a national search to find a slate of people with the credentials--and I'm sure they will. And that's the way it should be done. At any rate, when it came down to the final interviews, I remember being interviewed in the Department, and one person asked me: "Why would I want this job." I said, "I never said I *wanted* the job." And he said, "Well, would you consider doing it"? And I said, "Well, I would consider doing it. I think it's a critically important job and if I'm asked to do it, well, I don't see how I could refuse to do it." And that's how I got it.

Harden:

First, let's talk about a number of topics with which you have dealt. Coming back to the financial problems. Not only has budget growth slowed but, first, I'd like to talk a little bit about the intramural program and its impact. You have a very low gross budget if any at all in the intramural program. And, in addition, Congress has now removed the mandatory retirement age for the federal workers and a number of people have commented on the so called "graying" of the intramural program here. How do you view these phenomena and its impact on you and your investigators--being able to anticipate a career intramurally?

Wyngaarden:

Well, the intramural program has participated in the budgetary growth at

exactly the same rate as the extramural. In fact, it doesn't appear that way because. In fact, it appears the reverse because as the budget is formulated each year and the President's Budget Message, the percentage growth of the intramural program is almost always greater than the extramural. The intramural program has, in a way, only one advocate and that's the Director. The extramural program has a thousand advocates and they testify before Congress and many special interest groups that are pushing this disease and that development. And in the end, Congress adds money to the President's request. They rarely add money to the intramural program. So, the Director has to be the advocate for the intramural program. But what happens with this process, and this is just by chance, and exact parallel in the growth of the two components. And, a few years ago, when we were being questioned about this by one of the extramural groups, I actually got the figures together and at that moment the extramural program had gone 114% since the index year; the intramural, 111. That close. So, it has grown and I indicated there has been an overall 2 to 3% growth rate of the entire--and that's growth after correcting for biomedical inflation. And we come out about 1-1/2 to 2% greater than the CBI. And a 4% year of inflation nationally, 5-1/2 to 6% inflation, in the scientific column. And, even using that deflator, there is that kind of a growth record. Now, we did lose purchasing power during the last several years of the Carter Administration. NIH had to withstand a 14% loss of purchasing power between 1979 and 1982. And that's the moment I

happened to arrive in '82. And there was a general sense that we were likely to be level budgeted or maybe less for the next number of years. In fact, Ed Rall and I sat down after my arrival to make contingency plans for cutback of intramural program. Fortunately, we never had to do it because there was a turnaround and then inflation was brought under better control and Congress added substantially to the NIH budget to the President's Request, and we've actually had a doubling of the NIH budget from 1972 to 1979 and that is an overall real growth of about 35 to 40 percent. Real growth rate, again corrected for biomedical inflation of about 5% per year on average during that time. Slowing this year. Last year it slowed a little. But we had a few years when we had 13-15% increase. So, overall we've had very, very good support in the last seven years but again we've had ever-increasing competition for these funds extramurally and the award rate keeps dropping. I mentioned one year when it was over 90%-- that was during the Eisenhower administration. The overall average has tended to be about 45-50% for the last ten to fifteen years. But it has been slipping since the early '70s. And it's been in the high thirties for most of those years--37, 38 percent. Then 31; probably around 28 this year. We project around 23 for next year. So, it's becoming very, very competitive for extramural support. We are about one billion dollars short, even though the budget this year will be over 7-1/2 billion dollars, we are about one billion dollars short of paying 45 to 50% of approved awards at the full amount recommended by Study Sections. And are paying full cost for

Centers; full cost for contracts. We've had to cut back, funding partially, in order to keep them going. That is not a lot of money in a budget as large as the United States budget but there are so many calls on it that we are that much short.

Harden: With the demand for funds, especially in the institutions across the country in the extramural programs, a number of people have suggested that we should just close down the intramural program and make this like the National Science Foundation--just a funding agency. What's your opinion on the value of the intramural programs?

Wyngaarden: I've heard that, too. I must confess to being very annoyed when I hear suggestions like that. That seems to me to be the ultimate in selfishness on the part of certain extramural people who resent the competition and some of the special advantages the intramural people have. But these jobs are packages. The intramural people do have a better access to research funds and they have less distractions with teaching and administration. But they give up other things including advantages. The salary here is substantially less than the extramural community and it's getting worse every year. And they put up with a lot of government restrictions that may not apply elsewhere. And, I have no sympathy for that point of view whatever. I was really pleased when we asked for a review of the intramural program by the Institute of Medicine that that Committee cited the extraordinary talent at this institution. And the manner in which that talent can be mobilized at times--and the AIDS epidemic is a good

example of that--to do things that the extramural community couldn't do or couldn't do as quickly. We were deeply into AIDS research--AIDS virus research--for about two years before the extramural community got much involved in it. There were a lot of reasons for that lag. Part of it is the slowness of getting additional funds and activating the mechanisms and the application process review and award process which takes time. But another part of it is that extramural scientists are reluctant to move from what they're doing into a new area until they're sure that the original area will be supported and that these are "add-on" funds. And there's a barrier to rapid movement into a new area that doesn't exist intramurally and we had substantial effort in the AIDS research field before there was really that much extramurally. But now, of course, it's very active in both places. But, there is, it seems to me, not only a defense, but a critical need for both components--intramural and the extramural. This intramural component acts as probably the largest single collection of scientific talent in the world. And it can do things. There's a collaborative spirit here that's hard to duplicate. There are some research intensive centers outside that come close but we also have a training function. And we have a public service function that, I think, is critically important to this area to foster and to protect and to promote and I tried to do that in every way I knew how during my time here and I trust the next Director will, also.

Harden:

What direction did you try to see the intramural program going more towards the proposal that NIH would become a private university or to

maintain it as it is within the government. What is your personal view on all of this?

Wyngaarden: I, of course, never favored the privatization plan as it was interpreted that the intramural program would become privatized to the extent of being outside of government and supported by other funds. That's competitively with the extramural program. I think it should be supported by direct appropriations, as it is. But, I think the idea of some kind of university status at NIH is very attractive. This institution has played a major role. Educationally, there are quite a number of graduate students who get their degrees from other institutions but do some of their research work here and I think NIH could be a small Rockefeller-type institution, a graduate university, smaller in scale of high quality awarding graduate degrees and we are continuing to work on that possibility.

Harden: I'd like to return to the subject that you raised a minute ago of the NIH response to AIDS. AIDS had just been identified in the summer of 1981 before you arrived. What was your personal response as a physician to this potentially-still for a while new disease--and could you describe a little bit about your response--Building 1's response--to how this could be managed intramurally. It's not a lot, but...

Wyngaarden: The disease had been described just before I arrived. But at the time, there were five cases in Los Angeles, or some very small number. And I don't think that we recognized at that stage what an epidemic this was likely to become. But, early on I think the physicians here interested in

immunological problems were absolutely fascinated by that phase of the problem. We actually have had patients in the Clinical Center in the '70s who almost certainly had AIDS, the late '70s. It wasn't recognized at that time. And there was work going on in a number of areas in this Institution, as you know, predominantly in the Gallo laboratory in terms of virus research. And Tony Fauci's group and others on the immunological side. And a lot of collaborative work between the Cancer Institute and Allergy at that time. And those laboratories got intensely involved in this probably very early. A predominant amount of early progress really came from those laboratories. There were other places as well. The Montagnier, group [at the Pasteur Institute] was early active as well. And Max Essex in Boston and others. It wasn't just here.

But, the intramural program got into this act very quickly and there were many conferences held to try put this fragmentary information together and see what way it pointed in terms of potential etiological agent. It wasn't all clear to everyone that it was a virus early on. Although from that first conference, people thought it probably was. At least it behaved like some other diseases known to be virus-induced. So, yes, I know we've been criticized for not getting into this more rapidly but early on the directions were not that clear. We didn't know the nature of the disease; we didn't know the etiology of it; and, also, we didn't have special appropriations for it. The first year or two we really didn't have to transfer funds to do this. And one of the things that Mrs. Heckler did during her

time as Secretary was to realize that we were really in an untenable position politically not to ask for specific funds for AIDS research. And from that time on we've had support for AIDS programs. In fact, only this year, the '89 budget, did we run up against the ceiling, as it were, and we didn't get everything that we asked for. Although it's still a very healthy budget.

Harden: You asked Dr. Robert Gordon to coordinate these early efforts intramurally and then I'm not clear--just if you don't mind clarifying this for me--whether he also was working with various Institutes to set up grants programs or whether they were working independently.

Wyngaarden: He was doing coordinated work to make certain that I was well informed of everything that was being done. The actual funding, when it was earmarked finally for AIDS, was primarily directed to the Cancer Institute and the Allergy and Infectious Diseases Institute. Then, with time, many other Institutes became involved also. The Heart Institute became involved quite early because it had a major responsibility for the blood supply--the safety of the blood supply for transfusion purposes. After Bob died, I asked Tony Fauci to serve as a trans-NIH, to organize a trans-NIH coordinating committee and designated that Institute as the lead Institute. Later, we elevated that mechanism to a special office in the Office of the Director and with an Associate Director in charge of it. And we gave Tony two titles. He's remains the Director of the Institute and also is an Associate Director for AIDS Coordination.

Harden: Thank you. Now, if AIDS was one of the great things with which you had to deal as Director, the proposed mapping and sequencing of the human genome is certainly the other.

Wyngaarden: Yes.

Harden: A number of scientists have questioned this whole project. Do we really need it? They've maintained that the work will be done anyway. What is your position and that of the NIH on the human genome project?

Wyngaarden: I think we need it. I think it has very high promise and I don't think the work could be done any way. The work on individual genes and interests is being done and will be done any way. But the identifiable genes constitute only a small fraction of the human genome. Even allowing for all the duplication of certain of these genes one might, at best, account for a third of the genome. There's still two thirds that would be unaddressed by that approach. And the scientific judgment of the best geneticists is that there is a lot of information in the rest of that genome otherwise why would we have it. And that there will be important insights to be gained from a systematic exploration of the structure of the human genome. Insights that should teach us a great deal about the biological systems, about development and differentiation, normal development and differentiation of the differences among human beings. But, in addition, provide new insights with relation to the disease mechanisms. The kinds of genes that are likely to be addressed because they are of special interest are the ones that are associated with specific proteins. Proteins. Specific

proteins. Or specific Mendelian-type of genetic defects. And there are many diseases in which there are hereditary components that don't follow these classic Mendelian patterns. And we can cite hypertension or manic depressive disease or any number of others--certain cancers that may be multi-genic. And in which there must be subtle play between regulatory genes and structural genes. I think it's infinitely worth doing and in terms of scientific project, it is really not that expensive. We expect this to level off at something on the order of \$200 million a year. We're spending four times that now on the AIDS project. And it should also be a finite program, completed in about fifteen or twenty years and, I suspect, at that point there may be no longer a need for a special human genome effort. It can phase back into the categorical institute.

Harden: Another issue that holds both promise and problems--two sides of the same coin--has been the biotechnology revolution that has brought government and academia together. Would you comment on how this has--the problems it might have caused you as Director and how you think the thing will work out.

Wyngaarden: Well, I think the biotech industry is a direct outgrowth of the research that has primarily been supported by NIH. The dividend on that genetics research was done in the '50s which was primarily bacterial, bacteriophage research at that time without any idea of what it would contribute other than additional knowledge. And, I think it is an example of a commercial development based on fundamental life-science research. It has spawned

a new industry and an important industry, one in which, at present, at least, the United States has a substantial lead over the rest of the world although competition is increasing from Europe and from Japan, in particular. And I think it is a very important contribution. As a matter of fact it adds a second dimension to the argument for the support of biologic science. The first of these is the fact that to improve the health of the human race and actually goes beyond that, to the animal kingdom, as well. At least the health benefit. And insert in there now, the commercial benefit. All these new products that can be made through biotechnology and are being made--new ones every day of the year. Now, it has also brought some new stresses. The possibility of getting rich in science has put a very particular torque on the system. And, it's a mixed blessing. I think the idea that science can be made more useful to these developments is good. The idea that scientists may have motives distorted by the commercial possibilities. If it is not contained in some way, could be a bad thing. That development has introduced a certain amount of secrecy in research. There are scientists now who are reluctant to talk with colleagues about their work. That had been one of the traditional hallmarks of biological science, and science, in general. It's international; you tend to talk with colleagues; you're related in similar work wherever they are, whatever country, whatever the laboratory. Now an element of caution and secrecy has crept into this. And in some laboratories it's very impassive. They won't discuss their work even in the corridor with

colleagues. I don't think we have much of that at the NIH. Probably a little. But it certainly does exist in the university world with colleagues have commented about that. The developments of engineers to hold a new series of issues--some of them are problems but not necessarily *that* problem. And we do allow intramural scientists to consult, for example. And that is responsive to the new congressional directives to facilitate technology transfer. And as federal laboratories and federal scientists, we're involved in this process. We have set up a series of guidelines and conditions under which that consulting can take place. And I think we have, up to the moment, had no particular serious infraction of those. Only something on the order of a hundred of our scientists are serving in that capacity of consulting and getting some consultation fees from this. And, for the most part these are small sums of money. You get an occasional person who is in very much demand and makes more. But, so it has not acted as a general boon to all the scientists at the NIH. But, I think it has helped for us to retain some of the ones who would otherwise be very much in demand in industry. We have a new series of conflict of interest issues that we're doing and we're feeling our way through that and I think successfully, so far. But, it does help occasionally science and it adds a new dimension and a new cultural warp that I think we have to watch closely.

Harden: Recently, in the last year or two, the question of fraud and misconduct in science, fraud and misconduct, has been in the news because of the

congressional investigations of specific cases. There are charges that the NIH is not policing its own, that nonscientific boards perhaps should be set up to do this. You, of course, are in the center of it all, as the Director. Would you talk about the problem?

Wyngaarden: We the first case of misconduct was referred to us in 1980, '81. The first NIH investigative panel was in 1981. And following that we had an increase in the number of potential events reported to us over the next three or four years, but since that time, it's been essentially level. We have about twenty such events per year. About half of these as we looked into them disappeared. Misunderstandings. Very trivial. The other half are of some level of importance and what happened to those are egregious infractions and serious events. So, we don't know if that's the actual total. There may be many others that are unreported and unrecognized. But, I would call attention to the denominator. We support 52,000 scientists through the NIH mechanisms and twenty cases reported to us per year, I think, must, just on the face of it, represent the highest ethical standard of any profession that you can identify in the United States. We're well ahead of the Congress; we're well ahead of the lawyers. And, nevertheless, it is a serious event because the pursuit of science rests on the premise of discovering truth. And betrayers of the truth do the enterprise enormous damage in terms of public support and congressional support. And we can't tolerate that. And, we have, I think, dealt vigorously with the cases that we felt warranted that. I know Congress has

been impatient and, to some extent, unbelieving that science can police itself. But if we don't do it, who will? This is not the kind of enterprise that subjects itself to random audit. That would be destructive of the fabric and fiber of science and the culture of science to move in that direction. As you know, I have in the past year, greatly expanded the office dealing with issues of scientific misconduct. We've moved that into the Director's office. We have given it 8 FTEs; two years ago, it only had two. And we've given the Office of AIDS more. And we're becoming much more vigorous in investigating those issues. Intend to work off the backlog. Some of these cases are complicated; do take a long period of time to finish, but I think we're making good progress with that.

Although, I regret in a way, the fact that NIH has had to get into a regulatory area, I think it is unavoidable. I think it's irresponsible for us not to do so and to expect some other mechanism to do it. I think in the long run would be very damaging. But we have a number of these areas starting with the Recombinant DNA Advisory Committee. Well, in a way it started before that with Animal Regulations and Human Subject Regulations and then the RAC, and then misconduct in science, and respective interests in certain areas of biotechnology. So, we have a number of areas in which the NIH has regulatory functions to perform. Not really regulatory in the sense of the FDA or EPA but nevertheless they are monitored, surveillance functions and we have to gear up to that and do it appropriately.

Harden: Another problem that has grown more and more strident during your directorship is the question of use of animals in medical research. And I recently heard more from Senator Lowell Weicker speak on behalf of a group lobbying to educate people about why this is necessary. How real a threat to biomedical research are the animal rights activists? What has been your experience?

Wyngaarden: They are a very serious threat, and the people who are addressing the use of animals in research are really actually a coalition of many individual groups. Some of them have exactly the same objectives that we have. To improve the quality and care of animals, the humane use of animals, reduce the number of animals where that is appropriate. Find alternative methods where that can be done. We are making good progress with that. On the other hand, I don't foresee the day in my lifetime, maybe never, in which one can forego the use of animals in research. Computer stimulation and tissue culture methods all have their limitations. One comes to the point when one has to study an integrated system, mainly an animal and some of these studies can be done on humans and *are*. But only when it's appropriate to do so. And necessary to do so. This large group of individuals might be called the Animal Welfare Movement. I think Animal Welfare is one thing, and we subscribe to it. On the other hand, the Animal Rights Movement has become a buzz word for all those groups that in the past would be called antivivisectionists and really want to bring the use of animals to a total halt. And, they are using

much more sophisticated tactics than they did in the past. It's tougher. They are taking a legal route, a public relations route and an educational route. They are making serious inroads into the grade schools and youth groups to condition them to become strident about the use of animals in research. And we're not, for a moment, defending the use of pets in research. We don't do that. Most of these animals are purpose-bred or they are animals that are going to be put to sleep in the pound anyway and those animals can be used for meaningful biomedical research. These groups are well organized and well financed; they have expert legal and public relations advisors; they have large memberships. I continually told people you have to assume there's a PETA member in every laboratory. *People for the Ethical Treatment of Animals* is one of the large coercion groups. You have to assume there's a PETA member in your own laboratory or at least in the laboratory next door. And that isn't all bad because I think we should be held to high standards. But these groups are just waiting for some perceived infraction to pounce on this. And their claims of abuse are greatly distorted, and they inflame the public--these are the sort of tactics they use.

Harden: A number of people have been somewhat disturbed that NIH has almost always taken a fairly low profile position in arguing the problem because of the emotional approach of the animal rights groups. How can science respond? Should scientists take a more high profile approach?

Wyngaarden: Well, I don't think they necessarily need a low profile. They've spent a

tremendous amount of energy on this animal issue and there have been times when we've spoken out forcefully. We have not been willing to defend what we think is indefensible and there have been some indefensible infractions. But I think we're still grasping for ways of reaching the general public on the issue of use of animals in research. And to some extent, advisors have felt that it's a no-win situation until the situation gets so acute that one can't avoid it any longer. We have, for example, had some public issues, public for fund; use of animals in research for science reporters. And we've had some public media personalities willing to speak on behalf of the use of animals. We've had children who've been benefitted by the results of procedures developed on animals, for example, open heart surgery. But the second day they withdraw. They speak to their agents and their agents persuade them not to do this. And so we've had some difficulty countering those public media people who come out against the use of animals in research with appropriate spokespersons of the same sort of degree of prominence. Those who have done so have been vilified. Nevertheless, I think that the tide is changing. We have, at present, in the Department, with Dr. Sullivan as Secretary and Mrs. Pointer as Undersecretary two people who are willing to engage the issues. Both have spoken out on the absolute essentiality of the use of animals in research and I think that we need to continue to seek that kind of statement from prominent leaders at and above the level of NIH. The Office of Science and Technology Policy has

played a role in that. And I think that it is now clearly time to carry this issue--public policy issue--to the people of this country. But, it's a delicate issue and it has to be done skillfully. It has to be done by knowledgeable people who are not eaten alive by the opposition, which sometimes happens, when one speaks only from emotion and not from the knowledge of the situation.

Harden: Another great political to-do was raised by the anti-abortion groups who opposed the use of fetal tissue in research. Using this as a point, how many of these single interest lobbies are there that affect NIH?

Wyngaarden: Oh, there are many. I don't know how many but there are many.

Harden: Perhaps we should come back to the fetal tissue issue as an example of one additional group in terms of how you, as Director, responded to this. What sort of a danger to research is this group and its proposals?

Wyngaarden: It is a very delicate issue and a very emotional one. It's not exactly the same issue as the abortion issue but it's related to it. And, there's no question that there are some disease states in which fetal tissue--human fetal tissue--has a potential for enormous therapeutic value. There's one pediatric syndrome--the George Syndrome, as it is called, it's an immunodeficiency state, for which fetal transplantations, are the treatment of choice, and it's curative. The work on childhood diabetes with fetal pancreas transplants is encouraging, and, we think should go forward. And with the use of certain fetal brain tissue in Parkinson's disease is still highly experimental. I think it is too early to say whether that's likely to

be beneficial but it has some promise and scientists are more experienced with it in Sweden, for example, than we do in this country, feel that the early work is at such a stage where they view this as a moral imperative to proceed. In our own advisory committee that we put together to look at all aspects of this issue, the Committee by a large majority took the point of view that they were not siding the abortion issue, that abortion was legal in this country within strict observance obviously. And that it was really a question whether the fetal tissue resulting from that procedure was being discarded, incinerated, or whatever, or whether some small fraction of it might be used to benefit other human beings. And the panel wrestled hard and long and it was a public panel and we had theologians on it from the major religious groups, we had public-spirited individuals on it and I think not only those who represent the Catholic institutions felt that you could not separate the use of fetal tissue from the abortion issue and they were opposed. Most of the others didn't take that point of view although there were some opponents of it that were troublesome to many other people as well. But they did recommend that that work go forward. It was a wrenching experience; it was for us, too, because many of us have qualms about such work.

Harden: I'd like to go back and pick up what we talked about earlier. About your personal upbringing, your religious, cultural, familial heritage. Would you comment on how your upbringing influenced your position on many of these highly controversial ethical issues?

Wyngaarden:

I think the background out of which I came will probably be closest to the Catholic point of view on this than my own view today. But part of my upbringing also stressed personal responsibility. I'm responsible for my own actions. Nobody else is responsible for my actions and I take that point of view here, too. And I apply that to the general concept of the right-to-life issue. I don't believe imposing my concept of morality or ethics on somebody else who doesn't think that way. Obviously there are limits to that but I think in this area we are in an area where I would apply that philosophy. I saw the other attempt as I was growing up. I was born during Prohibition and remember when Prohibition was abolished in 1932, I believe. But by the time it was abolished, the Mafia had become a major institution in this country and a lot of historians linked those two events. And I think that that's a very unsuccessful example of a Federal attempt to impose a certain morality on the people in this country. I believe that the Congress has taken much the same point of view. In fact, in the abortion issue, whether the public is in favor of the present situation depends to a large extent on how the questions are asked. But I think if the questions are asked in terms of restrictive use of abortion where there is a substantial risk to the mother if the procedure is not carried out, that the public supports this 2 to 1, as I understand it. Abortion as a form of family planning, I don't subscribe to it, at all. And I don't think that that's an appropriate use of abortion. I think there has to be some medical education. I would construe that rather generally. It isn't simply a disease

indication. I think the social, cultural, psychological part is also part of one's well being. And that would include that, and without putting too fine a point on it now, that's the way I come to this issue and I think that the use of fetal tissue generally flows from that point of view in my case.

Harden: You received some criticism, especially early in your Directorship, for travelling to speak at medical schools, because you obviously believed that there were some problems and that a liaison was needed. Would you discuss what those problems were and how successful you think you were.

Wyngaarden: First of all, I might point out, about 88 percent of our budget is spent extramurally. The NIH is the major determinant of the mechanisms and support of the biological sciences in this country. And our chief performers are the medical schools and universities. And also some of the free-standing research institutes. One of the things I discovered on arrival at the NIH was that Institute Directors and others were making authoritative pronouncements about the way things were in the medical schools with respect to NIH funding. And they weren't on target at all. They hadn't been there. And I came out of a medical school background. I knew the problems in the medical schools. I knew the gulf and understanding between intramural NIH managers and the medical school administration and the young scientists in the medical schools and the mid-career scientists and the problems they were having and so I spent a lot of time although it wasn't as much as you imply. I was selective in the opportunities that I accepted--the ones where I could reach a major

audience--major research society or I visited quite a number of institutions to talk and I think that that did help to quell what was a very, very anxious community. Bear in mind we were coming off that three-year period where we had lost 14 percent of purchasing power. It appeared as though we were going to be facing a level or less than level budget. Young people were abandoning research in medical schools. They would put in a grant application; they were not successful and they would quit. And there was a lot distress, obviously. There wasn't a perception of stability in these organizations. I worked very hard over this seven-year period to try to stabilize our mechanisms with longer terms of support, special programs for the young scientists who were emerging to bring it into the apparatus; career development awards; first awards; merit awards into this. And I think the situation is infinitely better today than it was then.

Harden: I know that developing clinical investigators has always been one of your top priorities. Do you think we can maintain them?

Wyngaarden: I think there's been some turn-around here. There was a declining interest for a number of years. And there are a number of statistics that indicate that there is a larger percentage of medical students now interested in research than was true in the past--who contemplate spending time in research. We have an increased number of positions in training; we have a slight upswing in the number of physicians submitting applications for research. I think, although it hasn't been a sea change, it at least has turned the corner and I think that the new programs and the same stability

that was brought to the NIH funding mechanisms have had an impact on that.

Harden: I've been going over a number of things that I've referred to as "problems," but we could also call them "challenges" that you faced as NIH director. There are a number of others that we could talk about--the constant pressures from the institutes, various lobbying groups, the problems that you've faced with the Inspector General over procurement problems that NIH was having. What has been your greatest frustration as Director with all of these challenges?

Wyngaarden: I don't know that there's been any greatest frustration. You'd have to press me a little on this, but I'd have to say that the greatest frustration has been the difficulties I've had with the Department and the procurement issue is just one of those. But it seemed to me many times that the function of the Department is to say "No." (Laugh) The things we've achieved have been achieved largely by the Congress. And I don't think it should be that way. I think that the Department could have gotten credit for many of these things had it been on top of them. Many issues. Part of that has to deal with the political process. It's a frustrating process. It still may be the best system in the world but we have as a result of political involvement a whole series of people who are brought into the apparatus on political appointments--some of them are excellent, but they're not uniformly excellent and I think there's a lot a jealousy of the NIH. The fact that Congress has treated this as a very precious institution, and has increased

its level of funding. It doesn't happen to many agencies. And there's a certain amount of jealousy at the relationships we have with Congress on many issues and a lot of that lack of empathy in the Department is just saying "No" to budgetary requests or tremendous delays in getting any kind of response. We had one memo, for example, on a Departmental misconduct in science policy that took 14 months to go through its various layers of the Department. During that time, we had this damaging hearing of the Dingle Committee where much of that might have been averted had that process been handled in, say, two months. It shouldn't take more than that. And these things just get lost in the internal procedures of the Public Health Service or of the Department, or OMB sometimes. That's been a very frustrating experience, but, as I say, it may still be the best there is.

Harden: Being NIH director, certainly, can be wearing on occasion. Nonetheless, you took it on.

Wyngaarden: Yes.

Harden: Do you consider that it has been a worthwhile venture these last seven years?

Wyngaarden: Oh, I do, indeed, think so. I wouldn't have missed it. I've enjoyed it and I have a lot of satisfaction out of the things that we've accomplished in this seven-year period.

Harden: During your confirmation hearings, you expressed a sense of obligation to maintain a perceived NIH standard of excellence. Looking back now, how do you assess your achievements and what do you think your greatest

achievement was?

Wyngaarden: I think the AIDS and the Genome issues that we discussed will probably stand out as the high points but in the larger sense, I'd say that I think the fundamental responsibilities of the Director of NIH are to acquire the resources for the scientific community to evolve programs and mechanisms that are as light-handed as possible and I've tried to do that to emphasize investigator-initiated research approaches, to involve the NIH as little as possible in regulating or making pronouncements and planning of science. I think we've done too much of that--requests for proposals, requests for applications. Because I don't have much confidence in our ability to tell the scientific community where the effective answers should come or are likely to come. We have to do a little of that because there are gaps but we have to do as little as we can possibly do. I think the stabilization of the mechanism has been an important advance. We touched on some of those, the mechanisms for attracting more young people into science, giving them the confidence they can get into the mechanism and do well with the supports there for a lifetime, and it is. The merit awards, I think, are a manifestation of that. When I came, 18 percent of all the awards we made were for five years or longer. Now that is close of 50 percent and we had about 16,000 total grants; now we're at 21,000. So, the apparatus has grown, not as much as we might have liked but I think those are important contributions. And, I think that the other side of this is to maintain appropriate surveillance and guidance in key

issues. We touched on those, too, the animal experimentation, human subjects, recombinant DNA, misconduct in science, conflict of interest, and, to date, we've had no restrictive legislation in any of those areas. For everything that we've done, although it's certainly not been perfect, has, I think, been adequate or sufficient, to meet the challenges. And, although Congress has had at us on some of these issues, they have yet to pass a restrictive bill in any of these areas.

Harden: The Congress has always been good to NIH, don't you think?

Wyngaarden: They've been very good. And, I'm not objecting to the oversight on some of these tune-up hearings. Although they have been painful at times, they have been beneficial. But I'm really pleased that we've been able to evolve mechanisms--at least to date--that averted any restrictive legislation.

Harden: As my final question, I would like you to speculate on what's going to happen in biomedical research in the next ten years? What challenges face your successors?

Wyngaarden: Someone said it's hard to predict, especially the future. I would start by saying that I think that the biological sciences apparatus in this country is very healthy and I believe that it has solid support in the mind of the public as expressed through the Congress and, indeed, through the Administration. This may be part of the strategy of not asking for too much knowing that Congress will add to it and the President has never failed to sign the Bill which the Congress has presented. So, I think that

the public support for science is very solid. They are the patrons of science and we have to remember that because we are accountable to them. Obviously, the apparatus has to be run very responsibly. But, I think that that's being done. I think it will continue to be done, so I'm very optimistic. I think there's a growing awareness of the vital contributions of science, in my case, bringing the life sciences to the welfare of the people and I am very optimistic that the support will be there. It should continue to be an exciting undertaking for anyone who has the talent to enter science. They should not be unwilling to do so. I think they'll find that the support is there to do as well in the future as we're doing now and have done in recent years.

Harden: Congress has been grateful to you and has expressed its gratitude a number of times. I thank you very much for talking with me.

Wyngaarden: My pleasure. Thank you.