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NCI Director Broder's Year In Review: Avoid Politics, Stay Focused On Science

NCI must remain clearly focused on its scientific mission to prevent and cure cancer, and avoid being drawn into political and economic controversies, NCI Director Samuel Broder said in an interview.

In the past year, NCI has been criticized on many different fronts—by activists, in Congress, and in the oncology community. ***The Cancer Letter*** *offered Broder the opportunity to put the recent events in perspective.*

Broder said he had no regrets about NCI's handling of two of the most controversial issues, the change of guidelines for breast cancer

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In Brief

Bruce Chabner, DCT Director, To Leave NCI Next Spring For Position At Mass General

BRUCE CHABNER, director of the NCI Div. of Cancer Treatment since 1982, will leave next May for a position at Massachusetts General Hospital. Chabner will head the Div. of Hematology and Oncology, and serve as clinical director of the hospital's cancer center.

"It is an interesting opportunity for me because of the vast patient population of the hospital and the remarkable confluence of scientific resources of the Boston area, including the hospital's cancer center, Harvard and MIT," Chabner said to the DCT Board of Scientific Counselors this week. "The move will allow me to rejoin several very close colleagues and friends and to pursue clinical research in a very supportive environment."

When he leaves, Chabner, 54, will have worked 26 years at NCI, 23 of those continuously. He is the third NCI division director to leave within the past 11 months.

"The walls of NCI do not stop at Wisconsin Avenue, but extend to all parts of this country," Chabner said to the DCT board. "I will remain a supporter and an active participant in its programs, its plans, and hopefully, in its grant-supported research."

Chabner said he would miss the young scientists who come to the Institute. "There is no better place in the world to work at the beginning of a career in research," he said.

"At the same time, I would be dishonest if I did not admit that the government is becoming an increasingly difficult place to work for a person interested in clinical research," Chabner said to the board. "You know of our problems with hiring and promotion freezes, declining budgets, and increasing

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Broder Reflects On NCI's Role, Handling Of NSABP, Screening

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screening in younger women and the Institute's handling of scientific fraud and mismanagement at the National Surgical Adjuvant Breast & Bowel Project.

In the interview conducted Oct. 12 Broder said:

•The debate over breast cancer screening guidelines was unnecessarily intense because health care reform entered into the controversy. Broder reiterated that NCI was not pressured by the Administration to make its decisions.

•NCI made numerous attempts to accommodate former NSABP Chairman Bernard Fisher prior to Fisher's removal.

•About 300 sites involved in the Breast Cancer Prevention Trial have formed a network that could stand on its own, separate from the NSABP.

•The budgetary outlook for NCI is expected to be austere until 1998.

•The NIH Clinical Center must remain a vital component of NCI's research program.

The interview was conducted by Kirsten Goldberg and Paul Goldberg.

CL: This year, on Capitol Hill, NCI has been accused of being sexist, racist, lacking commitment to breast cancer patients, being protective of the "old boy" network. What is it like to be on the receiving end of this?

BRODER: Oh, I think it comes with the territory. Our job is to prevent and cure cancer, and we have to keep focusing on that.

CL: Do you believe your predecessors had to defend the Institute so vigorously?

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BRODER: Sure. With any highly visible government agency, there are going to be times when the public expresses concern. What you have to do is respond to legitimate criticism, consider all criticism, try to adopt the spirit that a constructive level of criticism can improve performance and can enhance trust.

It is important to listen to the totality of criticism, not to turn it into a simple debate where individuals are keeping score. So if consumer advocates or members of Congress raise eight or nine criticisms, and if one or two of them are correct, we should act on that. We shouldn't say, Ah, seven of the criticisms were off the mark—we win.

People expect a lot from their science-based agencies. That's not new. Those individuals who were here during the creation of the National Cancer Program went through a lot of stressful times. Dr. [Vincent] DeVita [former NCI director] went through enormous levels of stress at varying points in his career. I think it's part of the expectation that anybody who does these types of jobs has to have.

CL: Is the tone of [the criticism] changing?

BRODER: I'm not sure Dr. DeVita would have seen quite the tone of it then. His biggest battles were over appropriations and over the environmental toxicities and the safety of the clinical trials program.

The public demands a great deal from its public officials. Individuals still turn to government agencies when there is a problem. Even if there is disappointment with the government agencies, they will still only accept a government agency's review and responsibility in a matter, and they will not trust anyone else.

CL: After several sessions on the Hill, I can't imagine it feeling too good to you, as a human being, some of the criticisms. Over breast cancer screening, for instance.

BRODER: In part, some of the difficulties we have faced represent a change in the entire climate of expectations over health care, health care reform, uncertainties as to what that will mean, and what individual roles will be played by each of the government agencies.

Everybody has his own viewpoint. There's a kind of Proustian point of view. Everybody looks at the same problem and will come in with a different interpretation of the same event.

I believe that the National Cancer Institute is best when it's fixed with three major foundation stones. And that's basic research, clinical trials and prevention, and in treatment, our cancer centers.

If you want to add within those three foundation

stones, a strong commitment to community service and outreach, and the whole agenda of cancer control, that's perfectly appropriate.

We're not a regulatory agency. Many people think of us that way, but I don't believe that's a good role for us. We should not be a reimbursement policy making agency. We are available to add our expertise, our scientific or technical knowledge.

We should recognize that when regulatory issues and reimbursement issues come into the mixture, we're in a situation where the special qualities we have can run into difficulties.

CL: Have attempts been made to push you into a regulatory role?

BRODER: No, but where individuals implicitly feel that what we say with regard to a scientific issue will have ramifications for some policy issue, then we're in an area where the message is under discussion, not its interpretation.

Our job is to be the one agency in the government that speaks to cancer, that generates knowledge with respect to cancer, and then helps apply that knowledge at all levels, including in a research setting, and in a community outreach, and a cancer control arena.

CL: Is that any different from what your predecessors might have said?

BRODER: I think that, by and large, they had less in the way of reimbursement considerations in many issues. There wasn't a national health care reform agenda where, what the NIH or any of its components would say, might be taken up and absorbed by third party payers, or by the government itself. In that arena we can get into difficulties.

CL: How do you protect yourself?

BRODER: There's no protection [other than reiterating] that our job is to generate knowledge, and to disseminate that knowledge, and apply it. That cannot be inhibited. We have to be cautious not to make promises on which we can't deliver.

We have to make sure that we limit our assertion of expertise to those areas where we really are experts.

CL: So the goal is to stay apolitical?

BRODER: I don't think science is political; at least I don't like it to be thought of that way. Science generates knowledge. What society chooses to do with the knowledge is far beyond our level of expertise.

I don't believe NCI should be in the role of making social policy. By the same token, NCI should be an unfettered and uninhibited source of saying the truth as best as we know it.

We have to draw a distinction between what we know and what we hope.

CL: You've been drawing that distinction and still getting quite a bit of heat for it. On mammography, for instance.

BRODER: Well, I'm still here. The National Cancer Institute is still functioning.

When you have these great moments and these great tides of expectations, I think you can't have it any other way, quite frankly.

In a democracy, there has to be a dynamic tension of ideas, and as long as everybody fights fair, there will be differences of interpretation as to what that knowledge-generating role is.

CL: If you would put this in a nutshell, what have you learned about the American political system in the past four and a half years?

BRODER: Nothing new has emerged in my recognition of the American political system that I didn't really already feel that I knew.

You can't expect the public to support an activity without expecting the public, or its representatives, to ask you to defend that. You can't personalize that, you can't get defensive about it, you can't interpret it as an attack on your professional standing. You have to take that as a expected given.

CL: So you've never asked yourself, "Is this what I went to medical school for?" after a particularly unpleasant episode on the Hill?

BRODER: No. Medical school is very useful because they give good courses in psychiatry. I don't believe you can be the director of NCI without having good credentials in psychiatry. I'm not joking.

Patient Advocacy, Funds Redistribution

CL: In your tenure, cancer patient advocates have become a major political force. On balance, how has this affected NCI?

BRODER: Don't forget—I was molded in the crucible of AIDS activism. So for me, this was the way of life I was used to. When you reduce everything to its final bottom line, what most activists want is to have their lives protected, or to have the lives of people they love protected.

Theirs is a very simple and extremely powerful message, and we have to be careful not to become sidetracked from the essential power of that message. And the moral authority of that message.

We can disagree on implementation. We can disagree as to what solution may be useful.

CL: Has there been a major redistribution of funds to breast cancer over the past few years?

BRODER: Well, breast cancer has certainly been dramatically increased, but that process is certainly not confined to breast cancer, and we've increased several different areas. Breast cancer is certainly one.

CL: Has there been a change in research priorities?

BRODER: Breast cancer, certainly, has been underfunded in the past, and we have to make sure that we keep the momentum going. But by the same token, prostate cancer was dramatically underfunded.

When I took over, out of a budget of $1.5 billion, the amount committed to prostate cancer was $15 million. You don't have to be a rocket scientist to say that's a radically imbalanced allocation.

Sometimes people adopt a certain way of analyzing a problem. They adopt an aphorism, and then that becomes a sort of given truth.

Lots of people would come up to me and say that you can't study prostate cancer because you can't get prostate tissues. That's ridiculous; that's absurd. It's one of those areas that's so absurd that you don't need to think about it.

What we've tried to do is address that balance without getting into unnecessary ritualistic battles over basic research versus clinical research. We need both to be strong.

The SPORE [Specialized Programs of Research Excellence] Program is still an experiment, we still have to keep looking at it, but I think the SPORE Program is a success, and in some ways is accomplishing more than we expected.

CL: So you're saying you have both now, you have a balance?

BRODER: I think the Institute has always had both. We have to make sure that there is a strong basic research agenda, but I think organ-specific research has an important role.

We have SPOREs in breast, and prostate, and lung cancers, and in gastrointestinal disease. I think they have really galvanized people, and, ironically, they're extremely cost-effective, because the act of putting together a SPORE application has had an effect.

I've learned that sometimes the act of asking for certain types of projects induces the formation of collaborations, even if a particular funding instrument is not given to an institution. They've gone through a process of becoming cohesive, and sharing ideas to put in the application, and they say—hey, okay, you're cool, we'll get together.

CL: Has the balance between undirected and organ-specific research been affected?

BRODER: The balance probably has been affected. The organ systems program was really going into its last phases when I first took over. I think if you want to, consider the SPORE Program as in a linear descent from the organ systems program. The SPORE Program accommodates it. It's a program that focuses around a particular organ site, develops expertise, develops interdisciplinary connections, forces institutions to make an institutional commitment to the field, and forces collaborations, including sharing of tissue.

We've been able to encourage people to tackle difficult problems. For example, I'm quite proud of the fact that we made pancreas a mandatory requirement of the gastrointestinal SPOREs even though we only have a limited number of them.

We did it that way because pancreas is a surpassingly important kind of cancer. We're not making substantial progress in it, and there's a potential risk to investigators who send in applications trying to tackle it. This particular review body would, perhaps unintentionally, have a tendency to prejudge the application and declare that it's unlikely to work—which is a safe bet.

But this gets us into a circle of, because it's unlikely to work, we're unlikely to try anything.

So we made it a condition, and therefore, the peer reviewers were liberated from having to assert in advance that it's unlikely to work. We already know that pancreas is a very, very tough disease. Now let's see what you can do about it.

CL: One frequently hears your colleagues, scientists, say that you've been too responsive to Congress, to the political interests, too willing to bend over backwards. What would you say to that?

BRODER: People have accused me of being too conciliatory? I hear the opposite. That I'm too rigid. I'm actually a little bit surprised to hear that because I think that for the basic scientific community, we've made a very strong effort to support the principle of investigator initiated research.

In fact, in fiscal 1992, we funded the largest number of new and competing grants in the history of NCI. We got the largest dollar increase that the NCI has ever seen. We need more, but certainly a lot of basic research was supported.

For people who are worried about clinical research, my belief is that you shouldn't just talk about it and wait for NIH [to form] study sections. If you add up [NCI funding for] the cooperative groups and the [Community Clinical Oncology Programs], they have risen about 54 percent, using 1991 as the base. The Institute as a whole has gone up under 25 percent.

Presumably these people are not complaining. I wish I could accomplish more flexibility.

CL: Some people would like you to get up on the Hill and say, "Congressman So-and-so, I'm a scientist and you're not, please leave science to scientists." Can this be done in the 1990s?

BRODER: But I've said that. You've been at hearings where I said that either in text, or subtext.

When the [Breast Cancer Prevention Trial] was discussed, as to whether it was advisable or not, I said, "I'm sorry, it's advisable. Breast cancer is a very substantial disease. We've analyzed this and we think it should go ahead." And that was the end of it.

As scientists, or clinicians, you only have standing within the domain of your level of expertise. So certainly, you can tell someone, where it's appropriate—presumably we'll do so tactfully—that "I'm a scientist and I'm a physician, and it's ill-advised for you to tell me which genes I should clone in sequence, or which drugs we should develop."

The Congress seldom does that; very rarely, in my experience.

You've been at hearings where the policy was attacked, and we didn't change the policy. So it amuses me a little bit when people say we're too conciliatory, or we bend too much. We don't bend. We don't go looking for a fight. I think there's a difference.

At all times, even when there is profound disagreement, the government agency must show a high level of respect for the lawful representatives of the people.

The Congress has a perfect right to say, "Are you spending money wisely? Are you obeying the laws in the pursuit of your mission? Is your procurement integrity good? Is your ethics training good?"

It's not our job to say, "How dare you do that?"

I'd like to see the areas where people have complained to you. Presumably they've given you examples, areas where we have bent in the face of congressional pressures.

CL: One hears this mostly [in connection with] the National Surgical Adjuvant Breast & Bowel Project.

BRODER: Well, I understand that. It is easier to think of some of the difficult decisions that one has to make in that light, and in some strange way it's more comforting than to accept the reality of what is happening.

It is more comforting to view it in the matrix of congressional pressure, and expediency. It's much more difficult to accommodate the realities and what the public expects from governmental officials.

It's easier to see a decision that way, and not to live with the reality of what the decision is. Or for individuals to critique that decision, to ask, well, what would they do faced with the same set of facts? Really, what would they do?

You can have a different point of view until you actually have to make the decision.

NCI Handling Of Mammography, NSABP

CL: There are two major controversies that brought you to the Hill this year. Mammography screening and the NSABP controversy. In retrospect, is there anything you would have handled differently in either of these controversies?

BRODER: It is generically true, presumably until you die, that most people grow with each day, and learn new things, and then can look back.

I don't know how much good that will do because no two situations ever are the same. Some people say history repeats itself. Well, it may do that, but it never comes back quite the same way, and you can't always know the exact lessons.

CL: To paraphrase Marx, tragedies return as comedies.

BRODER: Right. I think sometimes that is true, and I think sure, tactically, and from an operational point of view, we would perhaps do things differently.

But the core principles—I'm not sure we would have done anything differently.

In the case of the mammography issue, we had issued a promissory note in the late 1980s that we were going to make a policy decision to make certain recommendations regarding mammography. Because the clinical data were compatible with it, and a major randomized trial had been launched, and in order to make the best possible use we could, we were not going to wait for the trial to come back.

It was a very logical decision. Well, the trial came back. What are we then supposed to do?

I think the one thing you want from a director of NCI is that the individual will be bound by facts. Otherwise, if we're liberated from having to stick to facts, then anything is possible.

The issue with mammography is that somehow, there has to be a codicil to our earlier work. We have to convey the information that an expectation we had has not been fulfilled.

Because if you say you're going go do something, and you're going to be bound by the results of a clinical trial, and if you liberate yourself from both of those, then you really are opening yourself up to a situation

where anybody downtown could give you a call and say, "I don't like your policies; very inconvenient."

CL: You've been asked this question a thousand times, but can you say, unequivocally, that there was no pressure from the White House or HHS to change the guidelines?

BRODER: We had already undertaken a process while George Bush was still the President. There was a presentation late in 1992 to Peter Greenwald's Board of Scientific Counselors, giving the preview that the data were going to come out that mammography did not appear to confer benefit.

Now, you can always talk about the flaws inherent in the study; that's a different topic. A workshop was convened early in 1993, before a health care reform agenda came up.

The recommendations of that workshop came out a certain way. This isn't necessarily what I want, or what somebody else wants. This is the momentum.

Now, how do you tell the public there are these new realities? Are you going to adopt a position that the knowledge is too dangerous for the public, and that they shouldn't worry about it?

That's the other side of this implication. We're very comfortable with the American Cancer Society's position. They've looked at the same set of facts, and they've taken a different position. There's no problem with that.

CL: If one were to ask ten oncologists out there whether there was pressure, eight of the ten will probably say that there was pressure, even though you have raised your hand in Congress and said there was no pressure.

BRODER: The workshop was in February of '93. It had been organized late in '92—Clinton had not been sworn in.

CL: So it was just a coincidence?

BRODER: It was a coincidence in that health care reform zoomed in, and that's exactly the point I'm raising. Reimbursement issues started to kick in.

Let's take odansetron, which is a very effective agent for nausea and vomiting. If we do a study with odansetron and we find it is a superior performer in nausea, vomiting control, we have to be able to say that. There's a difference from making the assertion that odansetron should be reimbursable and should be the first agent tried in a health plan.

You never want a situation where somebody will call you up and find that the knowledge that you're generating is too inconvenient to some other larger public policy purpose.

So we actually got the opposite of that. A number of people were very concerned. We did not know how we should handle it.

A suppression of the Canadian results and the totality of the meta-analysis could have easily ignited a comparable discussion: What are your data? Why are you making these assertions? Why are you making claims that you can't defend? What else are you telling us that works, when you're doing so on the basis of an inadequate database?

We'd like to be in a position where we can tell anybody to get off our case, we have to tell the truth.

Saying that randomized trials to date have not shown a survival benefit between 40 and 50, when all data are put together, or at least that there's a substantial pool of individuals with considerable expertise who hold that view, is far different from saying, "I oppose mammography." Or that mammography shouldn't be reimbursed.

CL: So it's the timing of the mammography debate and health care reform that feeds the lore of the call from the White House.

BRODER: But that's true of many historical things. Don't get me started. If we weren't on the record, I'd give you my history of Europe. There are many historical things people adopt that this is what happened, only it didn't happen that way.

The facts are that we started this process in '92. You can't convene a workshop in February of '93, on one week's notice, on January 20th.

What made it very difficult was that everybody did that. They put it into health care. In a way, I view that as psychological projection.

Many critics needed to have our results come out a certain way to make their argument, and it was very convenient. So they assumed that we were doing it for the same reason that they needed it.

It's a classical psychological projection. You impute to people the motives that you have.

There are some individuals that need a result, or a policy, to be a certain way from their point of view, and therefore, they assume that you're stating a point of view to establish your own internally driven policy.

That wasn't what we were doing at all. But for a variety of reasons the debate got way out of the normal bounds, and I submit that if it weren't for reimbursement issues, the debate would not have had that intensity.

We're not having a debate like this over flexible sigmoidoscopy. We're not having a debate of this magnitude over PSA.

CL: Some critics would say the data weren't that clear, it wasn't like [clinical trials of] a drug, and the decision could have gone either way, but NCI chose to

err on the side of saving money rather than on the side of saving lives.

BRODER: No, that's absolutely not true. The original decision was based on a contract with society: We are going to assert a policy, because we're waiting for a study to come in.

I think there are things that an individual doctor, or individual patients know, or want to know, that should be left in their hands. I don't believe in having a giant algorithm of medicine practiced all over. It's my own personal belief, and I'm against the tide on that.

Having individual doctors make up their minds is very logical; having individual women make up their minds is very logical.

Where you get into trouble is where you say, "I've made a decision because the studies show it that way."

Where you get in trouble is when somebody says, "Why are you asking me to do this?" And then you say, "Don't worry about it; trust me; the data are too confusing for you."

Whatever we did, it would not be right. That's why I started by saying we're a science-based agency. You have the right to ask us why we're doing something and it should be a scientific issue. Occasionally we'll tell you, "Because, look, we honestly have the pros and cons, but intuitively, this is what we think you should do."

Mammography was one of those areas that we really cannot get our experts to agree. You can look at the data, any multiple which ways, but we did have this belief that a study was going to come back, and the study didn't come back the way we expected it to.

Now, you can always say there were problems with the study. You can always argue. And if you want to get into that discussion, that's okay.

All I'm asking is, if you're going to say in advance that you will only accept studies that come out the way you anticipate them, then say that that's your policy. Be honest.

Because that's like flipping a coin and saying I'm only going to accept tails.

CL: So this has been the range in which you tested the principle of NCI being a science-driven agency, the way you've just phrased it?

BRODER: Well, it's true in other areas, but people are not focusing on them. The same argument could be made for a lot of different things. I may be wrong, but I'm being consistent. It's basically the same way that I try to respond to any of a number of issues.

You won't find dramatic inconsistencies as to how we're approaching each of the things.

CL: To return to the NSABP controversy, do you believe that [former NSABP chairman] Bernard Fisher was treated fairly by NCI?

BRODER: I feel that Dr. Fisher was treated in accordance with the expectations that we have to have of our principal investigators.

Let me establish my bona fides with respect to Dr. Fisher. You may have been at the General Motors Award ceremony. I toasted him. I have participated in scientific award committees, which properly granted him major scientific prizes. We at NCI revere him. He's a major figure, and has been a major figure for the last 40 years.

But we cannot have a separate rule for major figures versus anyone else. I believe that over a period of time, Dr. Fisher clearly did not fill many of the administrative expectations that we had, in very serious ways. That's a major issue. We think we've offered a number of creative and constructive options for him, which he has not chosen to accept.

When it became clear to us that he could not be the principal investigator of a funding instrument because a variety of administrative issues that were not new to him, had been brought to his attention in a number of settings, he was offered a number of options—chair emeritus, scientific director in charge of program development. A number of things where his intellect could prosper and continue.

You can't say I want to be the principal investigator, but I don't like administrative stuff. The public has the right to know that people will be held accountable.

Our cooperative group program is one of the jewels in the crown of the NCI. Our clinical trials apparatus, along with our CCOP program, are unbelievably important mechanisms, and we'll do everything we can to support them and to protect them.

This is an issue that was difficult for us, but I believe the right decision was made.

I honestly believe that any person who had the responsibility and had to do the total analysis of what was going on would have come to the same conclusion.

CL: Do you believe that NCI was treated fairly, both on the Hill, and perhaps by your colleagues in the community?

BRODER: I think that individuals in many cases made assumptions without awaiting the full facts. Or sometimes took certain philosophical points of view that we really can't accept. That's an area where I cannot be conciliatory.

We cannot ever argue—ever—that fraud is somehow acceptable, or it's something that you have to expect in clinical trials.

I've heard people say that very thing to me, and

having completed the sentence, they then denied that they said it. It's very interesting to me.

CL: I'm sorry, what did they say?

BRODER: For example, they would argue that in any live study there's a certain amount of fraud. I would rephrase it and say, "You're saying that fraud is acceptable." And they would say, "That's not what I'm saying." But that was what they were saying.

They argue a sort of statistically-based rationale, which is that the purpose of a randomized trial is to correct for these matters.

They don't understand that this is not a statistical issue; it's a value issue. On this point there can be no compromise, because the compromise enrages the public.

We cannot accept fraud, and we cannot use as a defense that you can statistically correct for it.

Fraud is a violation of values. It is unacceptable across the whole waterfront. One, it's unacceptable because it's a rejection of values.

Two, you could have danger from it if somebody doesn't obey eligibility rules, and enters patients, getting them in the wrong setting.

Three, it might under some conditions, alter a result, in ways that you might not anticipate, degrade the power of the study.

It's certainly cost-ineffective; it wastes resources, if nothing else, because you are paying for things that are not valid. So you're in effect taking away from things that are valid.

And you're providing a strange competitive advantage to people. One of the things that happened with [St. Luc Hospital surgeon Roger] Poisson—he was the number one or number two accruer in many [trials]. But we now know why he could do that. He cheats.

An author is responsible for the content of what he or she writes. We received very strong assurances from Dr. Fisher that he would be writing a reanalysis, and as it turns out, that wasn't the case.

CL: Do you believe that enough is being done to unmask scientific fraud now?

BRODER: I think the primary responsibility is in the scientific community. The scientific community has to develop an abhorrence for this, make sure the people involved in research understand that that's not permissible.

CL: Once fraud is found, do you think that the mechanism of dealing with it, the mechanism of punishing it, the mechanism of investigating it, are adequate?

BRODER: I believe that the primary function of all of our mechanisms should be to prevent and should be to correct those institutional issues where an environment of fraud can occur.

The infrastructure requires accurate identification of problems, accurate reporting, accurate respect for the legitimate role of the grantor. Data are generated by grantees. It's their responsibility to conduct the studies; it's their responsibility to write it up.

As the events have shown, when something goes wrong, the public expects the governmental agency to fix it.

Then sometimes people ask for the invocation of a power which—having been invoked before the problem became apparent—would have been viewed as an authoritarian exercise.

One of the most interesting things that came out of the [Rep. John] Dingell hearing was Dr. Fisher's statement that he believed that he had fulfilled his obligation to both the grantor and to the drug company, in the case of the endometrial deaths by reporting it at the [NSABP] annual meeting.

That was an astonishing statement. It was certainly viewed as astonishing by the drug company, who actually admitted that they went to this meeting and still weren't aware of it, and they described what it was like.

This is a meeting with 1,500 people. Dr. Fisher, in his mind, actually believed that he was fulfilling his responsibility to notify the grantor and the drug company at this meeting. His organization had made up slides in the summer of '93. Clearly, at that point the information could have been disseminated.

Certainly somebody could have notified us.

CL: Some people have said we just don't have the resources to uncover fraud. Fraud is thoroughly concealed. Fraud is not obvious. You have to spend a lot of money to uncover it.

BRODER: Yeah, but that's not relevant to the major issues here. What is required is a common-sense application of what is going on. When a problem exists, our understanding is that you'll let us know about the problem. Don't wait nine months before you tell us.

Don't try to conduct a massive investigation. Without letting us know. Then, when another case comes up, don't not tell us again. And then get mad at us. Which is exactly, literally, what happened. It was as though nothing had been learned.

Don't tell us you're going to publish a paper, and then have us patiently asking you, "Can you please let us know, whatever?" If you say you're going to reanalyze, reanalyze promptly. Do it. Don't give us thousands of reasons why not. If we ask that you review your auditing procedures, maybe eight charts, pre-

identified, is not enough. Don't get defensive and write us all sorts of things that you're not going to do.

If we ask for the establishment of data safety monitoring boards—they have a very valuable function. They're to buffer you from having to deal with a bureaucracy like us.

Don't tell us, no, we're not going to set up data safety monitoring boards, except when we want to, which is what NSABP did, basically.

CL: But the argument one hears is that this is a waste of money, to be spending all of this on scientific fraud, which is rare, and since it's rare, just randomize—

BRODER: But nothing I've said really costs money. As to the issue of just randomize, that's extremely unwise, because first of all, you are wasting eligibility. Second, there can be situations when there can be harm, and that's not a trivial issue. The same mindset that makes up eligibility criteria can introduce lab values that are made up.

You're asking too much of the randomization process to correct for all problems, especially when there are occasions when only small differences are what we expect.

I think people are arguing points that we're not asking to be done.

The irony is that the vast majority of our cooperative groups have complied with these requests and are doing just fine. We do not have a generalized problem. That's one of the points I made to Congress.

CL: Is the problem confined to NSABP?

BRODER: NSABP is by and large the dominant problem area that we have had. I think they've done a real good job recently in trying to fix it up.

This is not a widespread problem. Most of our cooperative groups are phenomenal. They're efficient, they respond to the data, they keep their audits going. They've been doing that for years.

NSABP was, in one year, three standard deviations below what the standards were. In all fairness, people made an allowance for Dr. Fisher that might not have been made for anyone else. We can't do that anymore.

CL: What do you see as the future of NSABP? Can it survive in its current form?

BRODER: Well, some aspects of NSABP, most assuredly. Our tamoxifen prevention study will survive insofar as we have any ability to deal with it.

On this point, Leslie Ford [chief of the Community Oncology & Rehabilitation Branch in the Div. of Cancer Prevention and Control] has done a phenomenal job. She's put together approximately 300 sites.

They have formed their own network. Many of them are NSABP sites, but they're operating as a prevention operation. They're very good, they're very dedicated, and I feel very confident that this process is going to continue.

CL: It could stand on its own?

BRODER: It will stand on its own.

CL: Away from NSABP?

BRODER: It will stand, one way or the other. If it's within the umbrella of the NSABP, that's fine; but it is not going to be tied to any future eventualities related to NSABP. This study is important to the National Cancer Program, and we will make sure that it survives within our ability to make sure that anything happens.

CL: Is this in any way tied in with the research-base CCOP application from [Pittsburgh Cancer Institute]?

BRODER: One of the things that I believe has been under-appreciated is that the Univ. of Pittsburgh and the Pittsburgh Cancer Institute represent formidable research institutions. The Biostatistical Center at Pittsburgh is a major national resource.

Also, some independence of the Biostatistical Center versus the [principal investigator] is desirable. I don't think it's mandatory. But some moderate professional independence is something that we should encourage. That hadn't been the case within NSABP. You have documents that clearly indicate that.

So the Biostatistical Center will have its own issues, and we welcome NSABP. We want to be as open and as interactive with the process as we possibly can.

We want to be helpful. I did go to the [NSABP annual meeting at] Opryland Hotel [last June], which was a learning experience for me, as I'm sure it was for the 1,500 people in the audience. I didn't do that because my schedule was light that day.

It wasn't a pleasurable experience. At the beginning, I was rather disappointed with some of the questions I was getting, quite frankly.

CL: The call for resignation?

BRODER: That part I rather liked. I think there was an unwarranted anger at individuals who were identifying problems, and there was very little in the way of asking, or at least entertaining the possibility that NSABP participated in this whole issue, and there were things structurally inherent to NSABP that needed to be fixed. There was that lack of self-examination.

I don't think we're known for massive, capricious, arbitrary, emotionally-driven decisions. My rhetoric is not filled with a lot of hyper-emotionality, usually.

I lose my temper as much as the next person. But there aren't a long list of irrational start-and-stop

decisions. Basically, we're a pretty conservative organization. When we take steps that are unusually decisive, it might be good if people would just take two steps back, and keep an open mind that there are facts that will come out, or that should come out, or that are a part of the issue, that are relevant, and are not trivial.

The Future of NSABP, Tamoxifen Trial

CL: Can we go back to the PCI CCOP question? I have heard that it is entirely possible that the PCI CCOP may be the future home of NSABP.

BRODER: I wouldn't rule it in, or rule it out. We have a job that has to get done. The reason we have cooperative groups is not to benefit the physicians, or people that work in the cooperative groups. The primary beneficiaries of our cooperative groups should be the patients in the study. That sounds pompous, but that is how I feel.

That is why we get appropriations. The money is supposed to benefit those individuals. If we have a study that has to get done, it will have to get done by the people that are the most expert and qualified.

There will be a type II competition for the research-base CCOP that currently is being used to anchor the prevention study. That due date is Aug. 25, 1995. We're not going to change that date. We will expect applications. There is no entitlement here.

The obligation is to the study. Leslie has in effect created a very substantial, powerful group of individuals. They're excellent. They're highly dedicated people. They're serious. They understand the issues. And they work through the DCPC; they work through Leslie.

We will find ways to support them.

CL: What about the rest of NSABP?

BRODER: That's why I went to the Opryland Hotel. I want to focus everybody on the future. I feel that it is very confusing when individuals say that only Dr. Fisher can keep the NSABP together. Only Fisher. Am I the only one that picks up on that?

CL: I've heard that.

BRODER: But does anybody understand the full implications of that statement? They don't understand. If they said that to a peer review group—

CL: What would happen?

BRODER: I think the peer review group would probably be astonished at the statement, and would certainly take it into account. And legitimately so.

CL: When you split up the PI and the chairman's responsibilities, what are the implications?

BRODER: Well, let's be cautious. The Biostatistical Center has been part of the unified [NSABP] headquarters grant. It is the bulk of what we're talking about—the auditing, the implementation. That's a highly technical, professional function. That's to go through peer review. That's not open to a popular election.

People will have to do the hard work of applying, sending an application, and showing that they're the best group.

We may split off the headquarters function and allow a traditional headquarters function to move with the chairman.

What we've made very clear to the executive committee of the NSABP is, though we do not have the right to tell them who to elect as the chair, they cannot designate PIs. And we expect them to follow certain national standards in their search, even though we don't have the right to tell them how to do it. Reasonably accepted national standards.

That is, a reasonable amount of advertising, some conscious outreach activities, some specific activity to try to identify women and minorities. Even though it's not our process, we're still going to have to defend it. We've asked them to apply those standards, and believe they're trying to do that now. *Editor's note: the interview with Broder took place before the NSABP Executive Committee elected Norman Wolmark, a surgeon at Pittsburgh-based Allegheny General Hospital, chairman of the group (**The Cancer Letter**, Oct. 21).*

CL: Is there anything else that needs to be said about NSABP?

BRODER: I'd like to say something in general. We will have strong, surgically-oriented cooperative groups, one way or the other. NSABP has been a phenomenal resource for us, and I really hope that NSABP can continue to function as NSABP. But we will encourage outreach to other surgical groups. We've received feelers from surgical groups that want to apply. I believe the American College of Surgeons has a planning grant to put together new groups.

I think the competitive process is the best way to solve this issue.

CL: So if NSABP goes away...

BRODER: We will have another surgical program. No matter what happens. NSABP is going to have to find its identity, and make a case for peer review. There can't be a continuous cross-referencing to prior achievements, and, quite frankly, I think the NSABP has done that.

You wouldn't allow basic scientists to do that. Everything is based on the present, and a strong, vigorous peer review.

The cooperative group program in general is going to be healthy, is going to be as protected as we can. It's going to have innovative uses of CCOPS. I'm very optimistic about the cooperative groups.

The Future of NCI

CL: That brings us to the next question: Looking into your crystal ball, how will NCI 10 years from now be different from NCI of today?

BRODER: It depends if we develop a cure for cancer... From 1993 to 1998, we have an interval where the Congress is faced with discretionary caps. We won't have all of our needs met.

We'll try and fight for as much as we can. Every few years, we do get recognition of some things. Fiscal year 1992 was a good year. We have to do what we can to bring that back. Having said that, [for FY95] Labor, HHS had a majority of its programs either fall, or go dramatically below their expected needs.

NIH got the largest dollar increase in the Department. This is competing against things like Head Start and Social Security.

CL: So you think you're doing pretty well?

BRODER: No, I didn't say we're doing pretty well. I'm saying that illusions don't help people, and we have to know what the reality is at all times. As we strategize for how we can get more resources, we need to understand the background we're moving against.

We're going to have to make our case in ways that are not viewed as simply making promises we can't deliver, and at the same time, that we recognize the length of the effort that's required.

We need a very durable commitment. We can't predicate a request for resources on: "If you only give us X amount, we'll give you an answer in two years." It doesn't work that way. We have to have a long-term commitment.

Our biggest problem is to get through this period of austerity, which probably won't end until 1998.

CL: Regarding the balance between the intramural and extramural programs, is NCI going to be the place that will spearhead scientific advances through the intramural program, or will this be a place that will primarily fund extramural research?

BRODER: Both. The intramural program is extremely important, but I don't believe it can be cast as a competition between the intramural and research project grants, or other mechanisms.

I think they are all important. The intramural program should focus on doing those things that it can uniquely do.

The clinical research component of the intramural program is extremely important. It may be more important now than it ever was, because there are many different issues related to high-technology, high-risk clinical research.

It's important for the programs here to examine everything they do, and to make sure that they are filling niches that no one else is filling.

The intramural program needs to work out a system where virtually everybody of good will recognizes that it's filling an important role.

That's easy to say; harder to do. We have to look at individuals in the intramural program, and we have to have good input from our peer community.

Especially, we have to preserve those clinical research issues that are hard to do now, and that many places just can't afford to, or find the climate is too difficult for them.

CL: Such as?

BRODER: For example, the things that [NCI Surgery Branch Chief] Steve Rosenberg does, the IL-2 studies, certain types of high-grade technologies, such as the alpha emitter, isotopes linked to monochrome antibodies. Certain aspects of AIDS drug development.

CL: There is a Clinical Center in [the Institute's future]?

BRODER: The Clinical Center is one of the most important components of the NIH. It's more important now than it was when it was built. The Clinical Center is not going away. I haven't heard any credible clinical researcher advocate the dissolution of the Clinical Center.

I think people have advocated a careful look at cost containment, and mission priorities. Most people understand the Clinical Center is much more important now, in an environment where managed care and other things are working very difficult burdens on people.

Many of the people in our cancer centers, and our cooperative groups, are functioning under heroically difficult conditions. They feel under-appreciated, but they are doing a phenomenal job.

I have some concerns about managed care. Managed care is having an effect on our academic centers. I feel our academic centers are put in an unfair situation, because they have to take care of very difficult cases.

We have to figure out ways of helping institutions through that.

CL: How is working with [NIH Director] Dr. [Harold] Varmus different from working with [former NIH Director] Dr. [Bernadine] Healy?

BRODER: Dr. Healy came from a discipline

involved in clinical research, and so many of the issues related to clinical research are second nature to her. Dr. Varmus, of course, is one of the most formidable intellects of our time, and is a basic research-oriented person.

Many of the clinical issues are not things that he knows first hand. So it's a different perspective; it's a different emphasis.

CL: How does that affect your job?

BRODER: It affects it as to what priorities we have to explain. In a basic research agenda, he will have it thought out before I have, so there's very little I have to explain, or could contribute to what he already knows.

In a clinical research issue, and particularly how to translate things from the lab to the bedside, there are a lot of things that we share, and he's very receptive to. But you can't take for granted that he will automatically have them as second nature, as he would a number of other areas.

That's one of the areas that we all have to work on. If you're involved in something every day, it's second nature to you, and sometimes you don't even know the first principles you have to examine.

The theory is often that basic research leads to clinical research advances, from lab to clinic, and I think we have to recognize that there are lots of times when the direction goes the other way.

Broder's Three Greatest Accomplishments

CL: What would you say have been your three greatest accomplishments as NCI director?

BRODER: I am gratified at the ability to improve opportunities for clinical researchers in multiple formats, including some of the newer mechanisms that we've developed. The R21. The R03. A modified use of the R29. Certain RFAs that were written in very generic ways to invite clinical research, and the very dramatic increase in our combined CCOP plus cooperative group budget, almost a doubling against the growth of the whole Institute—54 percent versus 25 percent [since 1991]. I'm very happy with that.

If I had articulated that as the goal when I got sworn in, if I had said we're going to double the commitment [to clinical research] people would have doubted it.

The SPORE program has been very gratifying to me, because I think it's ironic, when people who were opposed to it or had reservations about it, now come up to me and ask when it is this going to be expanded.

CL: And the third?

BRODER: I tried to create the view that the staff people working at the NCI, irrespective of their specific assignment, are critically important.

The staff here, whether they're in grants management or working on an intramural project to clone a gene, they're all doing incredibly important things. They should be proud of what they're doing, and their ideas are going to make a difference.

For example, the Cancer Centers Program. One of the things people were concerned about when I took over was that we were going to somehow damage the Centers Program.

The Centers Program, in fact, has been revitalized. The staff were liberated to be real partners. They've revitalized the program. They did it with their own creativity.

You only gave me three, but the comprehensive cancer centers program is something I'm very proud of. The staff deserve a lot of credit for that. People have now accepted the criteria, are seeking the designation, even though there's no money attached to it.

That's something I feel really good about. They are functioning the way comprehensive cancer centers should. They're not in this tremendous argument that informed the decade of the eighties.

Hopefully we can maintain the momentum as government becomes reinvented.

CL: How long do you foresee staying in this job?

BRODER: Why? Do you want to offer me a job? That's a difficult one for me to answer. I don't know. I'll let you know.

Chabner To Leave NCI In May

(Continued from page 1)

bureaucracy and politics. People like myself spend a great deal of time on committees that devise plans for getting what we need from an increasingly rigid system.

"The option to devote myself to issues that I think are of primary importance is my reason for leaving," Chabner said.

Chabner came to NCI in 1967 from medical residency at Yale to fulfill the military obligation. After two years as a clinical associate, he returned to Yale. He came back to NCI in 1971 as a senior investigator in the Laboratory of Chemical Pharmacology. He became head of the Biochemical Pharmacology Section in 1973, and chief of the Clinical Pharmacology Branch in 1976. From 1980 to 1982, he directed the Clinical Oncology Program.

In 1982, Vincent DeVita, then NCI director, appointed Chabner DCT director. Earlier this year, two other DeVita appointees left NCI: Barbara Bynum, director of the Div. of Extramural Activities and Richard Adamson, director of the Div. of Cancer Etiology.