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Broder: Cancer Act's Special Authorities Don't Give Director Immunity From NIH, HHS

The National Cancer Act, which was signed into law 20 years ago this December, gives the NCI director certain authorities that no other NIH institute director enjoys, including the ability to submit a professional needs budget directly to the President, and the authority through the President's Cancer Panel to identify impediments to the National Cancer Program. NCI Director Samuel Broder, in the second part of an interview with **The Cancer Letter,** (part 1 was published in the Sept. 20 issue) discussed these "special authorities," which were created in a compromise

(Continued to page 2)

In Brief

House, Senate Enact FY '92 Budget Bills For NCI That Differ By $200 Million; Senate's Is Higher

HOUSE AND SENATE have acted on bills for NCI's FY 1992 budget, approving two very different amounts that the conference committee will have to reconcile. The House approved $1.83 billion for NCI, a $116 million increase over FY91 (6.8 percent). The Senate, on the other hand, would give NCI $2.01 billion, an increase of $296 million, or 17 percent, over the current year. That amount would come closer than any in recent years to NCI's Bypass Budget, which requested $2.6 billion for FY92. "Naturally, I'm a little more enthusiastic about the Senate figure," NCI Director **Samuel Broder** told the National Cancer Advisory Board this week. The Senate voted down an amendment introduced by **Sen. Tom Harkin** (D-IA) that would have given NCI an additional $400 million. Under the House figure, NCI would fund 3,215 new and competing research project grants (32 percent of competing grants), compared to 3,073 it expects to fund in FY91 (29 percent). Estimates for funding under the Senate figure were being examined by NIH and not available by presstime this week. The conference committee was expected to begin deliberations possibly by late this week. . . . **NCAB APPROVED** unanimously a resolution commending both houses of Congress on their support of NCI since the enactment of the National Cancer Act of 1971. The resolution, introduced by Board member **Sydney Salmon,** urges the adoption of the Senate's figure, since it "would go a long way" toward realizing the Bypass Budget. . . . **NOTE OF CAUTION** was sounded by NCI Financial Management Branch Chief **John Hartinger**, who was queried by NCAB member **Bernard Fisher** as to his "best guess" on the final budget figure. "There have been rumors that we'd be lucky to get the President's budget. I wouldn't spend it yet," Hartinger said. The President requested $1.81 billion for NCI in FY92.

Special Authorities Aren't Immunity From NIH, HHS Chain Of Authority

(Continued from page 1)

between cancer program advocates who wanted NCI to be a separate agency and those who argued that taking NCI out of NIH would be destructive.

Broder cautioned against any assumption that the special authorities offer the NCI director "immunity" from the HHS "chain of authority." Broder also discussed NCI's relationships with NIH and FDA, streamlining of IND approvals, and personnel changes within NCI. Following is the interview:

CL: A big part of the thrust of some of the independent authorities in the National Cancer Act seemed to be to give the NCI director channels around the bureaucracy directly to the White House, public, and Congress. That was used extensively by Frank Rauscher and Vincent DeVita [former NCI directors]. They felt they had to invoke that authority because of what they perceived as road blocks along the way, and they took on OMB [the White House Office of Management & Budget], they took on the NIH director. You are probably much more aware than we are of what went on between DeVita and [former NIH Director James] Wyngaarden.

Broder: Do you feel it was successful?

CL: Vince may have won some points and he may have lost some. What he lost within NIH in terms of credibility or collegiality, we don't know. Maybe it wasn't worth the cost. What do you think?

Broder: I feel that there are some authorities that are very important and logical and scientific, and in a certain sense, noncontroversial. We owe a tremendous debt to the early '70s when these things became non-controversial. To me, the single most important, practical authority is the ability to publish a Bypass Budget. It's a unique trust that's bestowed upon the Cancer Institute.

We've tried to take that very seriously, and I've warned division directors that, except in an emergency, or some new scientific discovery, if it doesn't appear in the Bypass Budget, you've waived your right to ask for it. You couldn't come up with a new prevention and control study for $15 million a year that you haven't tried to defend in the appropriate Bypass Budget. It certainly will get scowls from me and probably one or two remonstrations at an Executive Committee meeting, and it's just something that we consider a negative mark against a division director.

I think that's a fundamental authority, a very powerful authority, and one that really has to be preserved and respected for the trust that it involves.

CL: You almost got the Bypass Budget funded a year ago before the Persian Gulf war came along.

Broder: I think it's instrumental in a lot of different issues, it clarifies the real intent of the Institute, it allows the public to participate in it and understand how we arrive at things, and I essentially tried to do the best I can to get people to recognize that there is only one professional judgment budget and it has to be predicated on professional judgment.

About two years ago, there was a proposal to have a Bypass budget and then to have a politically realistic budget. It can't work that way.

CL: DeVita tried that in about 1982 or '83, to come in with a "realistic" figure, so Congress gave him that and NCI still couldn't fund grants at recommended levels.

Broder: I believe that the Bypass Budget is realistic. We are not allowed to put pie in the sky figures in there. Everything in there is defensible. We can't operate under the assumption, just give us any amount of money. We have to be specific, we have to be professional, we have to convince the public and the Congress and the Executive Branch that the money, if it were available, would be well spent. It's not the same thing as saying, "If we don't get the Bypass, we'll take our marbles and go home." I think the mission of this institution has to be, "You can expect that we will do the very best job that can be done with whatever the lawful mechanisms of government give us as an appropriation." We will do our job. The Bypass Budget should not and cannot be used as some way of holding everyone hostage. Either give us the Bypass or we won't do the job. That's not the intent. There has to be an open and generous spirit behind it. I think we've been able to do that historically. But that's a profound act of trust and one of the most precious authorities.

That's the dominant one. There are some technical authorities that I think are important. There's printing authority, there's authority to name certain people on committees, and I think that those are all important, but those are hypertechnical things.

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CL: There also is the President's Cancer Panel, with the opportunity to go public when you need it. Evidently you haven't felt you needed to do that yet. Is that right?

Broder: I don't know what you mean by going public. Any institute director can go public.

CL: Well, if anyone else at NIH were to make a public statement that the HHS Secretary is not doing right by us, he'd be gone, or he could be. If you are at a Cancer Panel meeting, which is charged with finding out any problems, and the Panel chairman says, "Dr. Broder, what are your problems?" and then you say, "The Secretary is hurting us, because we need this and this or whatever." You're protected there.

Broder: Okay, recognizing that you gave that analogy, and recognizing that I did not. As you've described it, that's not a very productive use of the special authorities. I understand that it would fall within the technical abilities. I'm talking about the normal range of options in Washington. The structure of the special authorities of the National Cancer Program are not an immunity from chain of authority in the Department. It is wrong to create that fiction. The director of NCI is an employee of the Dept. of Health & Human Services, and an employee of NIH. The fact that it's a Presidential appointment is good. It gives certain types of moral authority to the position. But there are Presidential appointments in many areas of the government. They're still expected to report through channels. This doesn't mean that everyone has to be a company man or woman, and just take everything supinely. But you cannot create the literary fiction that the NCI director is somehow completely on a par with a Cabinet director, or is a special assistant to the President. I think that is a dangerous legal fiction.

CL: Probably the most effective use of the Panel in the past 20 years was Benno Schmidt's getting [Department Secretary] Caspar Weinberger's intent to kill research training overturned. He went public with it, he went to the White House with it--

Broder: Benno Schmidt did, not the NCI director.

CL: Benno Schmidt did because Rauscher said, at a Panel meeting, an open meeting, "Benno, we've got this problem."

Broder: I don't think what we're saying is inconsistent. I think it's a matter of what you're expecting to be done. I think that the theme of identifying problems and impediments to the National Cancer Program is not incompatible with the reality that the NCI director is in the chain of authority. I think it's very inappropriate to mix it up. It means you have less ability to get things done, not more.

I'm being as candid and as realistic with you as I can possibly be. The NCI director is endowed with certain special authorities, but the most important thing the NCI director is endowed with, presumably, is that person's credibility and perceived intellect, whether it's real or not. If a person's credibility, or powers of persuasion, or intellect do not carry the day, then attempting to invoke a special authority will not carry the day. The reason the thing was overturned, in your description, is because Rauscher was right, and had the power of the argument, not because he had special authorities. There's a fine line.

CL: You can say it wouldn't have happened if the problem couldn't have been made as publicly visible as Benno made it.

Broder: I'm not saying that there isn't a role for the ability to identify problems and to speak in an organized, formal mechanism. We are agreeing violently, as they say. But there's a nuance to what I'm saying. It's analogous to someone saying, "You come to me and tell me directly if there's any problem," in an organization that has a chain of authority. What one has to do is use that direct access as a synergistic mechanism, as a mechanism for helping identify the logic of what one is attempting to accomplish, but never to use it as a mechanism for asserting an authority in opposition to the lawful chain of authority. That's a nuance.

Though you may have cited an example where the special authorities have seemed to overturn a Secretary's opinion, I would have two points: One is, it is possible the Secretary's opinion might have been overturned by a direct appeal to him. Two, the public certainly would have found out about it anyway, because nothing is secret in Washington. I'm sure that maybe even **The Cancer Letter** would have covered it. And three, the bottom line is, it doesn't work. It doesn't work.

It's very important to be effective in this town, and it's very important to get the job done. Not to make compromises, not to bend on principle, not to be afraid to say things that have to be said, but it's very important to be effective. That's the most important duty that a person has. All NIH institute directors have their own professional judgment and can speak on professional judgment issues. We have very special authorities that are very useful to us and we have to use them for what they are intended to be used for. The example you gave might be a very good one, but you can't use them for what amounts to problem resolution within the chain of authority.

I think it's unwise to assume NCI can exist effectively without having a good, meaningful, practical working relationship with NIH.

CL: Do you have that now, do you think?

Broder: I think I do. I think that Bernadine Healy is an exceptionally gifted person. I think she's exceptionally sensitive to the problems of the National Cancer Program. But the point I want to make is that the program doesn't work if the NCI director is the only one looking out for it, furiously announcing problems to the President's Cancer Panel. It doesn't work. In that setting

if you want to fix that, you going to have to get an NIH director, whom we have, who cares about NIH and cares about NCI as being part of NIH, and will defend programs.

I think that's important to keep in mind: If you care about the National Cancer Program, you have to worry about who's the head of NIH. You can't just say, well the authorities of NCI will take care of it. It doesn't work that way.

I think NCI pushes the outside of the envelope of the total NIH. I think there's a lot of things that people are now accepting as valuable to NIH that were first piloted or started at NCI. I think the special growth for NCI in the era in which it was growing benefitted the whole NIH, and to this day, we have certain flexibilities that I think are very important, that can help the whole NIH community, across basic science, clinical trials, information dissemination, clinical announcements. We are ahead of the curve in so many different areas that other places rely on us for expertise. Our Science Enrichment Program [which NCI began last year] in which we try to develop scientific career potential in young kids from impoverished backgrounds. That's catching on, it's going to be an NIH initiative, maybe a Departmental initiative, maybe a government-wide initiative by the time we're done.

CL: Was that your idea?

Broder: Well, I don't mind taking a little credit. I think the concept of offering kids who are poor as the only criterion, other than their intellect and their character, and offering them a science opportunity, is something we should be doing. It can use science as a mechanism for ending poverty, which I actually believe in. I think people in scientific careers have the greatest opportunity to find advancement without having a social background, without being connected.

We, at NCI, were able to start that, with no red tape. I think that those are examples of things we can do, but it always has to be in the framework of NIH. We are part of NIH. It's a very serious mistake to somehow create illusions that we're not.

CL: How is your relationship with FDA?

Broder: I think they're great. I think FDA has got problems, as every government agency has problems. I think we have areas of disagreement, but I think we have an orderly process for resolving them. I think it's important to avoid creating the impression that everything that is wrong in cancer is somehow FDA's fault. That if only FDA wouldn't block our ideas, we could cure cancer. I wish that were true. I wish that I could just get into a ring with somebody at FDA and if I emerged the victor then cancer would be cured. It's not true.

Sure, there are areas of disagreement, but there will always be areas of disagreement. We have to work together. We don't always see eye to eye on various aspects of criteria for drug approval, for combination treatments, for off label uses. But FDA is made up of fine men and women who are trying to do their job. They're not out there saying, "How can we retard something, what evil can we throw at the system?"

We're not afraid to take FDA on, either from my office or from [Div. of Cancer Treatment Director] Bruce Chabner's office. On the other hand, I think we have to start with the assumption that even if we disagree, FDA is trying to do a good job, unless we have evidence to the contrary. We can't simply say, "FDA, in 1976 you screwed us up on cisplatin and adriamycin."

When I first took over, I said to people on my staff, there's a five year statute of limitations on grievances against FDA. Five years. You laugh, but that limited the grievances. A lot of the things that staff were coming to me with as areas that they wanted to engage in combat were from the mid-'70s, and I'm not making this up.

CL: That was mostly [former FDA oncology group leader] R.S.K. Young's doings, and he was gone by then.

Broder: I understand. I know the personalities involved. But you cannot atavistically maintain an administrative posture for one point in time. We don't do that with countries, even. We form alliances with countries that we used to bomb. We have to go on. The public suffers when one agency gets into a needless battle with another agency.

We've had certain ground rules. One of them is that we meet monthly with FDA. Our staff can go public on any issue that they need to where there's a disagreement, with one condition: Absent an emergency, they may not go public with a beef against FDA that was not presented to FDA first at one of these meetings. That's a rule that we enforce. Some strange things happen when you treat people with respect, and when you start with the assumption that they are trying to do a good job. They may actually respond to you.

CL: One of the early versions of the Cancer Act which was not passed included the provision giving NCI the authority to approve INDs.

Broder: I think that FDA is trying to be flexible in the IND process, I think they are trying to be accommodating. But many of the things we criticize FDA about are a reflection of the cancer community. There have been debates, not only going back to the mid-1970s, where in effect what FDA was doing was listening to an advisory committee made up of oncologists.

My point is, you can't attack FDA when what they're doing is legitimately trying to distill a sentiment of the oncology community. If the advice they are getting from the oncology community is bad, then you need go remonstrate with the oncology community.

CL: Do you think the IND approval process is

streamlined enough now that it's not a problem?

Broder: No, I think we still have some problem areas, but I think things are faster.

CL: You'd rather not do it yourself.

Broder: I think NCI is a scholarly organization. It should be generating knowledge. It should, when possible, avoid regulatory things. I'm comfortable with the situation in which FDA is responsible for regulatory issues. I'd like us not to become a regulatory agency. I'd like the whole NIH not to become a regulatory agency.

CL: Basically, CTEP [NCI's Cancer Therapy Evaluation Program] approves most of the protocols anyway.

Broder: We're trying to decentralize that. If clinical projects go through the R01 mechanism and go through a standing study section [see part 1 of the Broder interview, Sept. 20 issue], I've got an agreement with CTEP that if the project involves an experimental drug that we own, they will make a good faith effort not to substitute their own judgment for the judgment of the peer review community, in matters of study design. They will give great deference to the standing study section.

I know people feel suspicious about this, but CTEP will only intervene if there's a legitimate and good faith safety issue. Some people have said that gives us a net big enough to catch the whole city of Philadelphia. But I think [CTEP Director] Mike Friedman and all of his staff are reasonably informed about what we're trying to do. They have a lot of good faith in this matter, and they're looking to streamline things. We can't, however, club people for doing their jobs. We can't tell people, "You're responsible if anything goes wrong." And then at the same time say, "Ok, we want you to be flexible."

CTEP has been blamed for certain things. I know how frustrating it is for scientists, but we want to streamline it and we're looking for ways to streamline it. The R01 mechanism can do that. We want to decentralize INDs. We actually have proposals out that a comprehensive cancer center could distribute Group C drugs on its own. You know we didn't get a lot of enthusiasm for that. The record will show that that was met with very little enthusiasm.

CL: One center--Arizona.

Broder: The center directors probably talked to their attorneys. Whatever enthusiasm they had was completely wiped out. I'm trying to be a little facetious here, but I hope my point is coming through that people want certain streamlining from CTEP, and yet when we go to let other people assume the responsibility, there isn't enthusiasm.

We're working with FDA for both biologics and drugs to streamline the process. I come back to the theme that it's important not to blame FDA, unless they really are doing something. It has been more convenient to blame FDA than to say, "The oncology community isn't ready for a surrogate endpoint. The oncology community will only accept death as an endpoint, aka survival." We have to do a better job of convincing the oncology community.

Again, I'm not saying that we agree on everything, but even where we disagree, FDA has some logic in what they are doing. They're not just trying to stop drugs. They have a tough job to do. People shouldn't be blamed for doing their jobs.

At NIH, we get to go back to our labs. People get to go to important scientific meetings, and get to generate knowledge, and get to be famous. The FDA people have to work at Parklawn [Ed. note: one of the dreariest government buildings in the Washington area]. Among the penalties they have should not be abuse from us.

When we fight with FDA it should be [because] they've done something to significantly impair the National Cancer Program, not something where there's a lot of room for people of good will to come to opposing opinions. I'm not convinced that we were right in every battle that we fought with them.

CL: One thing we wanted to ask about is the stability in leadership of NCI--

Broder: You know how stable I am?

CL: You have division directors that have been in their jobs for 10 years, Al Rabson for 16. [On the Executive Committee, Deputy Director Dan Ihde is the only Broder appointee]. We're not suggesting you ought to push anyone out. The question is, does this fact say anything about your management style?

Broder: I've made very few changes in the Institute. I'm a low profile person. I think the best people you can find should be the people that run the place. I don't believe in making changes for change's sake. I know there are some leadership philosophies that like to shake everybody up and make people move around and all that. That as a goal of and by itself doesn't attract me. I think there could be a logic in having people take additional assignments back and forth, or to do different things as they grow tired or there's no growth potential.

Although the division directors have not been changed, they are doing some things differently that are not so obvious. They have different responsibilities now than they did a few years ago.

The Centers Program, which is one of the real foundation stones for the Institute, has been moved [from the Div. of Cancer Prevention & Control to the Div. of Cancer Biology & Diagnosis]. There's always room for improvement, but by and large the Centers Program is in extremely capable hands. Whatever criticism people may have now, the criticism that we ignore the centers program is not one that I hear very often or loudly. I haven't heard that people want the centers program represented on the Executive Committee as a goal by itself, because, as a practical matter, the centers program is very intimately represented on the

Executive Committee, by everybody, and by me. I think [Centers, Training & Resources Program Director] Brian Kimes and [DCBDC Director] Al Rabson love the centers program. They care a lot about wanting it to grow and succeed.

I think [DCPC Director] Peter Greenwald is doing some different things than he has done before. We are much more into the era of prevention trials on a large scale, and with Bernadine Healy's help, we are now able to envision and embrace important large scale studies in a way in that NCI does not have to assume the total burden of the trial.

CL: You're talking about the Women's Health Study.

Broder: Which is extremely important. But we've worked out a mechanism now where the various institutes in effect will pay their fair share of some trials. Instead of the theory of: NCI, you do it and if there are other endpoints besides cancer, we'll be there to give you advice, but you fund the whole thing. That was a significant burden. Peter is actually on assignment, in effect, not full time, to help us make sure that we get these studies done. He's doing things that are quite different than what he was doing before. Now, that doesn't mean there's a change of personnel, but there's a change of assignments.

CL: It is remarkable that this group of people has been intact for 10 years. You don't see that hardly anywhere. A few years ago the Dodgers had the same infield for eight years and that set a Major League record.

Broder: It would depend if they were winning or not. There are pros and cons. I think that you can get inbred. You can become jaded. A few points can be stifled.

There are a lot of staff changes at the level just immediately below the division directors. I think that's very important, and may actually be more important than the division directors or above. I think you see a lot of different faces in various programmatic levels. I mentioned Brian Kimes and the centers program, but you also have Barry Kramer in the Div. of Cancer Prevention & Control. You have a lot of new people in the intramural program, some of them have come in and worn a lot of different hats. Bob Wittes was a real good addition to our intramural program, though technically he is now at a lower level than he was when he left.

CL: He's back doing something he probably likes better.

Broder: He's doing something meaningful and important. He's a very excellent doctor. I think the intramural program is of surpassing importance to the entire national effort in many ways. You cannot have a healthy National Cancer Program without a very strong intramural program. It's not only my chauvinism, sort of having been reared in the intramural program. If you look at new institutes, what's the thing they are most obsessed about? Having a strong, visible intramural program. I think in the Cancer Institute, because the program is mature, investigators feel more of a sense of durability and security. They may not quite view the intramural program as being as important as it is--to them. But every grantee is made stronger by a strong intramural program, on a scientific basis and on a political basis.

CL: However, the intramural program has suffered [from tight budgets and turnover], too.

Broder: It has suffered, but on balance I think most of what is happening is positive. You can't have sudden cataclysmic turnovers. It was not a very good experience for us when Mark Lippman left and took 40 people [to Georgetown Univ.'s Lombardi Cancer Center]. That's a little bit too much of a good thing.

I don't like using military analogies because people take them the wrong way and it has a certain hawkish quality I don't mean to convey. But with that caveat, certain military operations have an inherent ability to recognize good young people and promote them quickly. That is the mark of a good general, actually, to identify the best field commanders and to give very quick promotions to those that can make it, and those that don't have to drop by the wayside.

I think the concept of having a national institution that can permit young men and women who are very talented, in a time of life when they have the tenacity and where they are not encumbered with a lot of distractions, to be able to obsessively pursue something and to pursue something that may have a large intellectual risk attached to it, is good. It's not necessarily a failure if you only retain people like that for five years.

By and large I'm not uncomfortable with the people and the turnover we have right now. I think about Eli Glatstein [chief of the Radiation Oncology Branch in NCI's intramural Clinical Oncology Program]. I've lost count, but Eli probably has populated five or six chairs of departments with his people. That's not bad. It's not bad for Eli, it's not bad for the people that have had that happen to them, and it's not bad for future recruitment. Because he can realistically say, "I can't pay you big bucks, but come work with me, you'll be chair of a department in five years."

Turnover, as long as it doesn't go beyond a certain point, creates opportunities for other people. I would include this office as part of that. I don't know, Vince wasn't really the longest in office.

CL: He was the third longest [eight years].

Broder: Third. There are some Institute directors that have been Institute directors much longer--17 to 20 years might be too long. The NCI system doesn't encourage that. I would think it would be a mistake for somebody to be the NCI director for 20 years. Why on Earth would you want that? You certainly wouldn't want to deal with me that long.

Tipping Resigned From ACS Post After Volunteers Expressed Disquiet

The sudden resignation of William Tipping from his position as executive vice president of the American Cancer Society occurred at a meeting of ACS officers in Chicago, when some of them expressed dissatisfaction with certain aspects of Tipping's management of the Society, **The Cancer Letter** has learned.

Rather than comply with demands that he pay more attention to recommendations of board members and the Society's volunteer officers, Tipping resigned, according to sources.

The official ACS position has been that Tipping was leaving "to pursue other interests." Tipping said in a written statement that he had accomplished his major goals in moving the Society's national headquarters from New York to Atlanta, overseeing construction of the new headquarters building, and reorganizing the national staff.

Gerald Dodd, current ACS president, added, in comments to **The Cancer Letter,** that Tipping had been working "very hard, in the move, completing the new building, and reorganizing the office. It is now all in place and represents a combination of achievements." That had required a "strenuous" effort, including recruiting replacements for those staff members who chose not to move from New York, Dodd said.

Tipping is in his 60th year, Dodd pointed out, and if he were to make a career change it would be to his advantage to do so now rather than later. ACS probably will attempt to recruit a younger person "who can stay with us for several years and give us some continuity."

The volunteers who were not happy with Tipping's management agreed that he resigned voluntarily and was not forced out. "It's just that we told him the volunteers were going to run this volunteer organization, and that we did not like the manner in which he was directing it," said one. "When it became clear that we insisted on that position, he decided to resign."

Tipping, contacted at his vacation home on Daufuskie Island, S.C., agreed that there may have been differences of opinion over some of the many changes he made in the organization.

"They brought me in when they needed a leader to bring things together, to make the move to Atlanta, to make other changes," Tipping told **The Cancer Letter.** "It worked out very well. Now, they and I agree that it is time for me to move on. I'm ready."

Tipping said that he has "no regrets. I think the Society is a better organization than it was, and I feel good about that. The Cancer Society is one of the premier voluntary organizations in the world, and I am delighted to have been part of it."

The Tippings have another home in Vermont and plan to spend some time there and at the South Carolina residence. "We're going to look at the options we have," he said. "Retirement, travel, take a look at what might come up."

Before becoming executive vice president in 1988, Tipping had been director of Hedrick & Struggles Executive Search Inc. in Chicago. He had served as a volunteer in the ACS Illinois Div. since 1972, was a member of that division's executive committee, and had been vice chairman of the national board and chairman of its Public Information Committee.

Mike Heron, ACS spokesman, told **The Cancer Letter** that Tipping's resignation "was unforeseen, but it was clear that his mind was made up." Heron noted that of the accomplishments Tipping had achieved in his three and a half years as CEO, "the one of which he was proudest was the strategic planning effort."

Tipping agreed and added that, "I also feel good about the staff training and development" the Society now has in place.

NSABP Seeks Investigators To Join Breast Cancer Prevention Trial

The National Surgical Adjuvant Breast & Bowel Project has released a program announcement requesting proposals from investigators interested in participating in the Breast Cancer Prevention Trial (BCPT).

The investigators should have a proven track record in recruitment to clinical trials, particularly through clinical cooperative groups, Community Clinical Oncology Programs, cancer centers, and similar mechanisms, and have an organization and staff experienced in quality control and data submission. To conduct the study, NSABP plans to designate approximately 70 centers throughout the U.S. and Canada to be responsible for recruitment, treatment and followup of women entered onto the study.

This study will determine whether long term tamoxifen therapy is effective in preventing invasive breast cancer in women at increased risk for the disease and whether the mortality attributed to the disease is reduced by tamoxifen. It will also determine whether tamoxifen lowers the incidence of fatal and nonfatal myocardial infarction and reduces the incidence of bone fractures.

Sixteen thousand women over age 35 at increased risk for breast cancer will be randomized between placebo and tamoxifen during a two year period. Women of age 35-59 years will be evaluated for eligibility to determine if, based on a combination of risk factors [number of first degree relatives with breast cancer; history of lobular carcinoma in situ; history of atypical hyperplasia; history of previous breast biopsies; nulliparity; age at first live birth; age at menarche] their risk of developing breast cancer is increased to at least that of a 60 year old woman. For each participant the annual and lifetime probability of developing breast cancer will be estimated utilizing a computerized model of risk assessment. The placebo or tamoxifen will be administered for at least five years. Toxicity and compliance monitoring, quality of life assessment, lipid and lipoprotein evaluation,

and other studies are major components of this trial.

This proposal must include the following documentation: 1) Verification that at least 50 women can enter into the study during each of the two years of accrual. The resources available to achieve these goals must be stated. 2) A detailed description of the recruitment strategy to be used. 3) Evidence of access to and commitment from agencies, organization, or individuals involved in the recruitment process. 4) A description of the organizational structure for ensuring adequate recruitment, treatment, followup, and data submission, including a contingency plan in the event of staff turnover. 5) Verification of the availability of staff with experience in recruitment and clinical trial care. 6) Evidence of adequate facilities for training, education, and internal quality control procedures. 7) Verification of the availability of medical staff (mammographers, pathologists, etc.) and the equipment and facilities necessary for monitoring enrolled subjects.

Applicants who may not be able to enter 50 subjects or more but who are highly desireable in all other respects are encouraged to pool their resources and submit a collaborative proposal with other centers in their geographic area. The final determination of approved centers will be made by the BCPT steering committee.

During the selection process, the steering committee will attempt to optimize potential recruitment by selecting centers most likely to make a major contribution. Consideration will be given to geographic dispersion of centers that will enable U.S. and Canadian women, particularly those from minority and underserved groups, to have ready access to participating clinical centers.

Investigators and staff from selected centers will be required to attend orientation and training workshops on recruitment, compliance, and data submission. On a quarterly basis, each center will be evaluated relative to recruitment and compliance; continued funding of each center will be based on successful performance evaluations.

Initial funding for centers (excluding CCOPs) will be provided via a subcontract issued by the NSABP. The amount of the subcontract will vary based on the institution's projected recruitment. When the original recruitment commitment is met, funding on a "per-case" basis will begin and will continue until accrual is closed. Funding for treatment and followup (on a "per-case" basis) will be provided for each ensuing year until completion of the study. The funding for participating CCOPs will involve the assignment of cancer control credit and funding through the CCOP grant mechanism.

To obtain an application contact Gladys Hurst, 914 Scaife Hall, Univ. of Pittsburgh, Pittsburgh, PA 15261, phone 412/648-9720.

RFP Available

Requests for proposals described here pertain to contracts planned for award by the National Cancer Institute unless otherwise noted. NCI listings will show the phone number of the Contracting Officer or Contract Specialist who will respond to questions. Address requests for NCI RFPs, citing the RFP number, to the individual named, the Executive Plaza South room number shown, National Cancer Institute, Bethesda MD 20892. Proposals may be hand delivered to the Executive Plaza South Building, 6130 Executive Blvd., Rockville MD.

RFP NCI-CM-27710-19

Title: Development of dosage forms & delivery systems for new drugs
Deadline: Approximately Oct. 24

The Pharmaceutical Resources Branch of the Developmental Therapeutics Program in NCI's Div. of Cancer Treatment is seeking contractors to develop dosage forms for compounds to be evaluated in cancer and HIV patients and to carry out innovative studies leading to more effective approaches for the intravenous delivery of compounds that possess limited solubility and/or stability. NCI will select and provide the compounds to be studied. In addition to solubility problems, the projects will require considerable analytical work, particularly the development of a stability-indicating assay to monitor the integrity of the parent compound during the formulation studies. These investigations will be directed toward a pharmaceutical dosage form that will meet certain solubility and stability targets predetermined by the Government. The Principal Investigator on this project must possess a PhD in pharmaceutics or medicinal chemistry and must have at least three years experience in development of injectable formulations. A portion of this project is a recompetition of two NCI contracts. The incumbent contractors are Univ. of Kansas and Univ. of North Carolina at Chapel Hill. The contract period is to be for five years beginning approximately June 1991.

Contract Specialist: Zetherine Gore
RCB Executive Plaza South Rm 603
301/496-8620

RFAs Available

RFA CA-91-31

Title: Mechanisms of Multistage Carcinogenesis in the Prostate
Letter of Intent Receipt Date: Oct. 1
Application Receipt Date: Dec. 20

The Chemical & Physical Carcinogenesis Branch, Div. of Cancer Etiology, NCI, invites investigator-initiated research grant applications (R01s) to elucidate the basic, complex mechanisms of multistage carcinogenesis in the prostate. New and experienced investigators may apply for funds to pursue investigations in animal and human prostatic epithelial cells. Project period may not exceed five years. Earliest start date will be July 1, 1992. NCI will commit $1 million per year to fund applications. Five to seven awards will be made.

Integrated studies are encouraged in: (a) cell biology and carcinogenesis, including identification of prostatic epithelial cells undergoing change; (b) carcinogen metabolism, including comparative metabolism, repair, and abduct formation between animals and man and from inter/intra individual donors; (c) molecular mechanisms, including molecular markers of change throughout transformation of an epithelial cell; (d) cellular mechanisms, including cell-cell interactions and responses to endogenous and exogenous factors; and (e) appropriate models, including suitable in vitro or animal models for prostate epithelial cell carcinogenesis.

Letter of intent may be sent to, and the full RFA received from Dr. David Longfellow, Chief, Chemical & Physical Carcinogenesis Branch, Div. of Cancer Etiology, NCI, EPN Suite 700, Bethesda, MD 20892, phone 301/496-5471, fax 301/496-1040.

RFA CA-91-30

Title: Understanding the Mechanisms of Hormonal Carcinogenesis
Letter of Intent Receipt Date: Oct. 1
Application Receipt Date: Dec. 12

The Chemical & Physical Carcinogenesis Branch, Div. of Cancer Etiology, NCI, invites investigator-initiated research grant applications to elucidate the basic, complex mechanisms of hormonal carcinogenesis. New and experienced investigators may apply for funds to pursue investigations on mechanisms of hormonal carcinogenesis in experimental animal systems, in vitro and in vivo, and in human tissues in vitro. Project period may not exceed five years. Earliest start date July 1, 1992. NCI will commit $1.5 million per year to fund applications. Seven to 10 awards will be made.

Goals of this initiative: 1) elucidate basic mechanisms of steroid hormone action that relate to the possible roles of hormones, particularly sex hormones, as carcinogens; and 2) provide a means to enhance multidisciplinary investigations, including consortial arrangements. Research could include studies on: 1) hormonal metabolites that could lead specifically to genetic damage or chromosomal malfunction; 2) karyotypic, cytogenetic and morphologic changes in models of hormonal carcinogenesis; 3) role of androgens, anabolic agents and progestins in hormonal carcinogenesis in organ sites such as the liver and mammary gland; 4) establishment of new in vitro experimental models for studying hormonal carcinogenesis in various understudied organ sites such as pituitary, testis, and uterus; 5) role of specific hormones in oncogenic process through use of transgenic animals or gene transfected cells; 6) molecular mechanisms of hormonally induced carcinogenesis.

Letter of intent may be sent to Dr. Lea Sekely, Chemical & Physical Carcinogenesis Branch, DCE, NCI, EPN Suite 700, Bethesda, MD 20892, phone 301/496-5471, fax 301/496-1040.