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Budget Difficulties Aside, Centers Important To NCI, Broder Asserts; Warns Against Sabotage

NCI Director Samuel Broder told cancer center directors that despite the lack of substantial budget increases for the Cancer Centers Program, centers remain important to NCI, and the Institute is planning ways to strengthen the program. But when a director questioned how NCI planned to fund several new initiatives involving the centers, Broder warned directors against sabotaging NCI's "innovations."

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In Brief

Simone Is AACI President-Elect; McGill, ICRC New Members; Engstrom ECOG Prevention Head

JOSEPH SIMONE, director of St. Jude Children's Research Hospital, Memphis, was elected president-elect of the Assn. of American Cancer Institutes at the group's annual meeting in Baltimore late last month. Simone received the majority vote over Albert LoBuglio, director of the Univ. of Alabama (Birmingham) Comprehensive Cancer Center. Simone, who recently ended a term as chairman of the Cancer Center Support Grant Review Committee, succeeds AACI President **Albert Owens,** director of the Johns Hopkins Oncology Center, which hosted the meeting. Two members were selected for the board of directors, **Robert Bast,** Duke Univ. Medical Center, and **Brian Henderson,** Univ. of Southern California's Kenneth Norris Comprehensive Cancer Center. They replace **Shirley Lansky**, director of Illinois Cancer Council, and **Marion Morra,** associate director for outreach/communications, Yale Comprehensive Cancer Center. AACI has 76 member institutions, and voted at the meeting to accept two new members, McGill Comprehensive Cancer Center in Montreal, Quebec, Brian Leland-Jones, director, and Institute for Cancer Research and Care in San Antonio, TX, Charles Coltman, director. The latter is a collaborative venture of the Cancer Therapy Research Foundation and the Univ. of Texas Health Science Center. . . **PAUL ENGSTROM,** vice president of population science at Fox Chase Cancer Center, has been named associate chairman of cancer prevention and control for the Eastern Cooperative Oncology Group. . . . **NEAL FLOMBERG** has been appointed scientific director of the bone marrow transplant programs of the Medical College of Wisconsin. He was an associate attending physician at Memorial Sloan-Kettering Cancer Center and associate professor of medicine and immunology at Cornell Univ. Medical College. He will recruit additional faculty in the areas of tissue typing, and prevention and treatment of infection and rejection. He also hopes to expand BMT therapy for solid tumors.

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'Don't Wreak Havoc On Innovations,' Broder Tells Cancer Center Directors

(Continued from page 1)

Broder's comments were made at NCI's annual workshop with cancer centers, held in conjunction with the Assn. of American Cancer Institutes annual meeting in Baltimore, MD, last month.

In constant dollars, the centers budget has fallen 15 percent since 1980. During the same period, the budgets for prevention and control and the cooperative groups fell 30 percent in constant dollars. Total NCI funding fell 6 percent, and, excluding money for AIDS programs, funding for the NCI intramural program fell 6 percent due to inflation.

"This poses some special problems," Broder told the center directors. "It is important to keep these figures in the back of our minds as we attempt to solve some problems." He stated, as he has in the past, that "a strong Cancer Centers Program is important to the National Cancer Institute." Yet, his discussion with the center directors implied that he could do little to improve funding for the program.

Centers have a major influence on reduction of cancer mortality, he said. "If you want to really make an impact against cancer, you really have to commit to prevention, and that means making a commitment to centers."

Broder highlighted two initiatives that will involve the centers program:

▶NCI would like to increase developmental funds contained in the Cancer Center Support Grants, or P30 "core" grants, in order to give center directors the flexibility to move funds rapidly into emerging areas of research or into innovative or risky areas.

▶NCI is developing a new center core grant using a seldom used NIH grant mechanism called the P50 that would be targeted toward creating specialized centers for research on breast, prostate, and lung cancer. Concepts for these "Specialized Programs of Research Excellence," or SPORES, were approved by the Div. of Cancer Biology, Diagnosis & Centers Board of Scientific Counselors recently (**The Cancer Letter,** July 5).

One participant asked where the money for the new P50 grants will come from. "It will be new money added to the cancer centers line. We won't take money from centers or research project grants," Broder said. He admonished the questioner, "Don't be so hostile. And don't use your inside knowledge to wreak havoc on the innovations we are attempting."

In a question and answer session, center directors indicated their concern about a few more items, and Broder provided the NCI perspective:

▶NCI has said that P01 grants are threatened due to a target on the number of grants NCI must fund (**The Cancer Letter,** June 21). P01s cost five to six times the amount of R01s, yet only count as one grant. "Why can't the projects included in P01s be counted separately?" a participant asked. Broder said NCI officials have asked NIH that question, and the answer has been that NCI's mixture of R01s, P01s and other grants were taken into account when NIH gave NCI its target grant figure. "The chain of authority says you can't change the rules in mid-game," Broder said. However, Broder said NCI remains committed to the P01. "We think P01s are important and we are not going to permit the numbers to drop."

Broder noted one reason NIH believes NCI is funding an appropriate number of P01s: "There is a perception that P01s have a lot of dead weight in them, and concern that we're not funding the best we can."

▶"Interactive" R01 grants have been proposed by NCI executives as an alternative to P01s. Under this mechanism, R01s would be submitted and reviewed as a package. Each of the R01s would count as a single grant (**The Cancer Letter,** June 21). The interactive R01 "would be especially useful for basic science projects, Broder said, while P01s are useful for projects with "a lot of lab to clinic translations."

"I hope you will not automatically oppose it simply because it is a change," Broder told the center directors.

▶Stimulating research through R01s. "We are trying to come up with a more user friendly approach to R01s," trying to get applications reviewed through standard study sections, specifically Experimental Therapeutics 2, Broder said.

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Over the past 10 years, while the RPG pool grew, NCI continued to rely on other mechanisms that remained level or fell, such as center grants, prevention and control, cooperative groups, Broder said.

"We need to explore mechanisms through which clinical trials can be funded by R01s," Broder said. "NCI does not have a user friendly mechanism for reviewing clinical trials. We're hoping to fix that."

The Cancer Therapy Evaluation Program has agreed that it will not "second guess" NIH study sections that review clinical trials and will consider peer review to be adequate protocol review. CTEP will review these protocols for safety issues only.

"We want a vigorous program of clinical trials," Broder said. "I'm very alarmed at the state of clinical research in this country. There are people who believe that if you want to do a trial you need to go to a drug company."

Commenting on the view of NCI within NIH, Broder said, "Other institutes view our problems with a mixture of sublime indifference to outright derision." Some institutes, he said, fund multicenter clinical trials as R01s.

Brian Kimes, director of the Centers, Training & Resources Program, later explained that those institutes, including the National Heart, Lung & Blood Institute, have formed their own study sections to review these types of applications.

Kimes said Broder has the authority to form such a study section that would operate under NCI. He provided no explanation why NCI has not taken this action, which presumably would eliminate the need to "reorient" the ET2 study section.

▶Proposed caps on cancer center core grants. Broder said he believes that, "In order for the centers program to exist and be effective it has to be based on excellence. We must have a system of peer review." Core grant review should be based on a zero-based budget, and not, as the program stands now, on a historical basis.

One feature of the P50 SPORES, Broder said, is that they offer a way to start over, with new money, placing all competitors at an equal level.

Broder promised that "we'll try to be flexible" in developing a cap based on the size of a center's research base.

"I really don't think we are going to have caps on cancer centers, but we need to institute the decision process in case money does not come in in the next few years," Kimes added later.

Kimes noted that cancer centers priority scores "bunch up in a very narrow range. It's very hard to say one center is worse than another." Usually, it is the clinical centers that are dropped.

Core grants are being funded at 81 percent of recommended levels in order to keep more grants alive.

NCI Is NIH's 'Administrative Reserve'

▶The annual budget process. Broder, emphasizing the budget constraints, pointed out that NCI is the only institute within NIH that lost funding as measured in constant dollars over the 1980s. "Where have you guys been? I only got here a couple years ago," he said.

A center director asked about the perception of NCI within NIH and Congress.

Broder noted that NCI's is the largest budget within NIH. "We're being disadvantaged because we're seen as an administrative reserve for any new program that needs to be done," he said. "Big budgets are seen as an administrative reserve and we are viewed as a big budget."

Funding for AIDS research is an example. "Not to say that those funds were not worthwhile," but money for AIDS research was earmarked and set aside without growth in cancer dollars, he said.

"The times are really very different," than a few years ago, Broder continued. "There were times when there was flexibility. There are now fiscal budget limitations, even cash flow problems in Washington.

"Even people who historically have been extremely friendly to NIH have expressed frustration that they can't find money. I wonder if some of the current stresses on NIH (scientific misconduct, indirect costs) are a guilt reaction of a Congress that can no longer support us."

Broder mentioned last year's House Appropriations Committee report on the NIH budget, which contained strong language resulting in some of the financial management constraints Broder now must work under.

"I feel that the people who do science are viewed as yet another interest group," he said. "I don't think Congress takes academic lobbying seriously. There are instances where pork gets in. But lobbying has been surprisingly non-effective. It has not been accompanied by a grass roots effort."

What is needed is a grass roots effort like that of the 1971 campaign for the National Cancer Act, Broder said, when columnist Ann Landers and philanthropist Mary Lasker "got real people to write letters."

"I don't think official lobbying is effective," he said. "I just don't see it happening. I think we need support from the public."

Later, Kimes told the center directors that NCI was doing what it could for the program. The FY92 bypass budget included $178 million for cancer centers. "We're doing our best as an institute to defend to Congress the program. We're doing our job," Kimes said.

"What do we do?" one participant asked.

"Sam [Broder] has been suspicious that the lobbying effort of the scientific community is not effective. Last year's House legislative language was the toughest language we've ever seen. It was shocking language.

"I honestly believe that if you were doing my job you'd do it the same way. We're trying to do our best for all centers." Kimes said he welcomed any center director to apply for a personnel exchange and join NCI to see for him or herself.

During the AACI meeting that followed the NCI workshop, participants pointed out specific instances in which they felt lobbying by cancer centers and academic scientists was effective. Invited speakers John Porter, Congressman from Illinois, former Congressman Paul Rogers, and Donald Henderson of the White House Office of Science & Technology Policy, encouraged cancer centers to continue to contact their elected representatives in Washington, to invite them to their centers and to state the case for cancer research funding.

Centers Branch Fully Staffed

Kimes and Cancer Centers Branch Chief Margaret Holmes began their presentations by marking a turning point in the program: the branch is now fully staffed, with four program directors and two support staff. Holmes is hiring one more support person. The program directors are Patricia McCormick, who came to NCI from the National Center for Nursing Research; Alan Schrier, from the Div. of Cancer Etiology; Linda Muul, who was in NCI's intramural program and the National Institute of Allergy & Infectious Diseases; and Blanche O'Neill, from NIAID's Div. of AIDS.

The branch is working on the following activities:

--The branch has formed a "solid working relationship" with the NCI Div. of Extramural Activities to improve peer review. All comprehensive centers will be peer reviewed when the two year time period for administrative review expires at the end of 1991.

--Revision of the core grant guidelines (see below). A draft has been sent out to center directors for comment.

--Working groups on database and prevention and control have been formed to advise the branch.

--The branch is "forging close relationships" with other groups within NCI, such as the Office of Cancer Communication, the Cancer The Cancer Therapy Evaluation Program, and the Community Clinical Oncology Program, Kimes said. "We're going to start becoming more active in promoting the cancer centers concept in those programs," he said.

--The branch is working on making the criteria for comprehensive cancer centers more explicit.

--Planning grants and "regional enhancement centers." With a stable budgets, it "seems silly" to plan new initiatives, Kimes said, but NCI needs to put some initiatives on the shelf in case funding does come through. Therefore, NCI will put out an RFA for four to five planning grants to states that do not have clinical or comprehensive cancer centers. Kimes is also developing a proposal for regional enhancement centers that would serve areas not presently served by NCI designated cancer centers (**The Cancer Letter,** May 17).

Grant Guideline Revisions

The Centers Branch is in the process of revising the guidelines for the cancer center support grants (P30s).

These are the main modifications:

--Under eligibility requirements, centers will have to have a minimum of $1.5 million in annual direct costs in peer reviewed cancer research support. The base may include most NCI grants and research contracts which support research projects, and grants from other institutes of NIH, American Cancer Society and National Science Foundation, and other organizations with high quality peer review.

--Under essential organizational characteristics of a cancer center, a new requirement was added to state that a center must have "a clearly identifiable major focus in cancer research." Other essential characteristics of a cancer center are: authority of a director, organizational capability and facilities, institutional commitment, and interdisciplinary coordination.

--The total amount that may be requested for all staff investigator salaries in a new or renewal core grant application may not exceed 20 percent of the total direct costs of the grant. This is down from a limit of 25 percent. These grants must have been awarded based on peer review. Holmes said 37 centers use this category.

--Comprehensive cancer centers may add another senior leadership position, that of an associate director for community affairs. This person would interact with community leaders to identify new resources and ensure that the research activities of the center are adding minority patients and special populations. Comprehensive centers also may apply for $15,000 to sponsor a conference on community issues.

--There will be greater flexibility in the use of developmental funds. Under the revision,

developmental funds could be used to recruit new investigators and support new investigators who have no grant support, as interim support for investigators, to develop new shared resources, and for feasibility or pilot studies.

--Institutional clinical trial protocols may use shared resources supported by the core grant, providing that the institution's system for reviewing and monitoring the quality of such projects is judged to be adequate by peer reviewers. Up to 20 protocols may use shared resources supported by the core grant. Holmes said the restriction to 20 protocols was included because, "We see a great need for support in this area, but we don't want the core grant to be swamped by one type of research. That may change."

Holmes said the proposed guideline changes would increase reporting requirements and require better recordkeeping on the part of centers. She emphasized that the modifications "are intended to include certain additional elements that are important to the success of the Cancer Centers Program." She said the revisions should be finalized by late summer or early fall and will require NIH approval. They should be in place by the Feb. 1, 1992 application deadline. Until then, anyone submitting an application will be reviewed under the old guidelines.

In response to a participant's question, Holmes said the branch is looking at the Veteran's Administration peer review system to decide whether VA grants could be included in counting a center's grant support for the eligibility requirement. "We want to look at VA peer review to make sure it is equivalent to NIH," she said.

Kimes said he welcomed written comment on the proposed revisions to the core grant guidelines.

Advice To Would-Be Centers

David Maslow, of NCI's Div. of Extramural Activities, provided some advice to cancer centers who want to compete for a core grant. These were his main points:

--Submit the application by the deadline.

--The application should be complete and accurate and contain all the required information.

--Follow the current guidelines and program advice provided at the pre-application consultation meetings.

--Be responsive to previous summary statements. Even funded centers applying for renewal should deal with issues raised in summary statements.

--Discuss any senior leadership position changes.

--Plan ahead for the site visit and set aside the days to host a review. Provide the committee with several choices of dates.

--Plan the site visit presentations carefully. More is not necessarily better. Allow time for questions. Unanswered questions hurt the applicant.

--Emphasize programmatic and interactive aspects in the applications, i.e., "centerness." "Show us how it all fits together instead of wowing us with the science," Maslow said.

--Allow time for tours and have escorts available promptly. Bring the core grant log books to the meeting.

--Provide summaries of usage of shared resources by each funded project.

--Address, either in the application or the site visit, the inclusion of women and minorities in clinical research.

--Encourage center members to help with reviews. Those who have participated in a review have a different perspective that helps in future applications, Maslow said.

Prevention & Control 'Not Equal'

Maslow drew some criticism on the review of comprehensive cancer centers when he mentioned that lenience was provided to centers on the cancer control requirement. "Having a plan was sufficient," he said.

"How are we ever going to get anywhere if [the prevention and control guidelines] are constantly diminished?" asked Shirley Lansky, Illinois Cancer Council. "They are not equal at all."

John Kovach, Mayo Comprehensive Cancer Center and new chairman of the CCSG Review Committee, said that in the review for comprehensiveness, "the committee found that the guidelines are not sharply defined." He encouraged NCI to refine the comprehensive guidelines.

Brian Henderson, Kenneth Norris Comprehensive Cancer Center at Univ. of Southern California, also spoke for an increased emphasis on prevention trials. "I'm concerned that the emphasis on community outreach will dilute the effort to do good prevention research," he said. Henderson urged that the guidelines be "as flexible as possible."

"Flexibility is fine, but you have to be ready for the committee to go the other way in that flexibility," Maslow said. On the comprehensiveness guidelines, he said, "they wanted more direction."

Ross McIntyre, Norris Cotton Cancer Center, suggested that some aspects of the revision seem focused on "trying to make review easy for the reviewers."

Another director called the guidelines "extraordinarily rigid" and said the workshop left him "even more confused." He said NCI staff approached these issues as "bean counters."

"I hope all of you will really look at the guidelines and tell us what you think, and if we're doing

anything good, then tell us that, too," Kimes responded. He complained that "it's only the negatives that dominate our ears. I don't agree that we are bean counters."

Later, Kimes added that, "we value your comments. We want your suggestions of how we can do it better."

Porter Says NCI Should Give Portion Of House Increase To Cancer Centers

NCI's Cancer Centers Program should receive a "substantial proportion" of the $20 million increase the House has provided NCI for FY 1992, Rep. John Porter (R-IL) told the Assn. of American Cancer Institutes at its annual meeting last month in Baltimore, MD.

Porter, a member of the House Appropriations Committee's Labor, HHS, Education Subcommittee as well as the House Select Committee on Aging, has been a proponent of biomedical research and cancer research in particular. Last year he called for full funding of NCI's bypass budget. "The work you do is very near to my heart," he told the AACI members.

Porter said the $20 million increase over the President's request of $1.81 billion for NCI is "nowhere near the bypass budget, but I feel reason to be pleased." The House amount provides NCI with a 6.8 percent increase over FY91, while NIH would receive a 6.6 percent increase.

He noted that historically, the NIH budget has grown at twice the rate of inflation, but NCI has not experienced the same growth rate. Since 1980, the NIH budget is up 27 percent in real dollars, while NCI's budget dropped by 6 percent. Porter called the difference a "33 percent discrepancy."

Why did this happen? "There has been a traditional concern that cancer research and NCI were dominating NIH's agenda and receiving a disproportionate share of the biomedical research enterprise. I don't want to get into that debate, except that in my opinion, it has reached the point where NCI should share equally with other institutes and in proportion with NIH."

This year, "Congress has turned the corner and we've acknowledged the disparity and eliminated it."

He pointed out that NCI received 40 percent of the $50 million increase that the House provided NIH. The committee did not specify any amount for the Cancer Centers Program, but Porter said, "I believe a portion [of the increase] should go to cancer centers."

The House passed the budget bill late last month.

Porter also discussed last year's changes in the way Congress does its budgetary work. Because of a deficit reduction measure passed last year, Congressional committees cannot move funds from one area of the budget, for example, defense, to another, such as health. Instead, this year, health programs are competing with all HHS, Dept. of Labor and Dept. of Education programs.

In the past, Porter said, "we could fully fund the bypass budget if we were to forego one B-2 bomber, but now we can't do that. Decisions this year are much harder." Some of those decisions involved "unemployment versus job training, versus student loans, versus elementary education." Even so, "the committee still kept NIH at a high priority."

Porter said he was concerned about the small increases in the Cancer Centers Program budget. The President's request for cancer centers in FY92, $114 million, "does not correspond with the description of centers program, which states that the Cancer Centers Program represents the most reliable and most effective research and outreach element of the National Cancer Program. The dollars simply do not match the rhetoric.

"Cancer centers provide the greatest link between basic research, clinical applications and community outreach. In my judgement cancer centers apply two of the most important missions of biomedical research--prevention and early diagnosis. You achieve the greatest results with a minimum of investment.... The success of the centers program is evident by the list of accomplishments: first therapy for leukemia, first curative therapy for testicular cancer, pioneered bone marrow transplantation, discovered tumor necrosis factor, the list goes on."

Porter closed by stating that the FY92 budget is an improvement over previous years. "We've turned the corner on equity among the institutes for fiscal year 92. We still need to get back up to the 1980 real level. We have not made progress on the relative importance of cancer centers within NCI. We need to continue to proclaim the accomplishments of centers, and Congress needs to continue to guide NCI to providing greater resources to the centers. I want to work with you this year and next year to accomplish these things."

'We Appreciate Your Coming To Washington'

Albert Owens of Johns Hopkins Oncology Center, which hosted the AACI meeting, asked Porter whether visits by center directors to Congress are helpful. "On the one hand, we feel that we have to develop that advocacy, but on the other hand, does our coming make a difference?"

"Yes, your coming is very effective," Porter said. "I'm always amazed that in this wonderful, free society of ours, many people in this country think they can't make a difference in public policy. I believe that

Congress and the state legislatures I know are mostly made up of caring, committed people trying to do a good job for the country or their state, making tough decisions, trying to make things work. People across this country have a great deal of influence as to how the policies are made. In fact, policies really aren't made in Washington, they are only ratified in Washington.

Writing letters to a congressman or testifying before a committee are important, Porter said. "Believe me, it makes a difference, in this place like no place on Earth."

Porter said he thought Congress has "done very well by NIH," providing a 27 percent real increase over the last decade, "far ahead of almost anything else. Military spending in America went up dramatically in the beginning of the '80s, but since fiscal 1985, it has been not only level funding, but has had a substantial real decrease. So we are able to make these shifts in priorities.

"We need you to tell us where to put the money and what we can hope to achieve. I think that captures the imagination of Congress and moves us in the right direction."

Sydney Salmon, Arizona Cancer Center, told Porter, "I'm very encouraged by what you say. For about six months now I have been a member of the National Cancer Advisory Board, and I wanted to point out that some of the things that the National Cancer Institute has done best have not fallen in what is called the traditional research project grant pool. For example, the cancer centers, the clinical cooperative groups, the things that bring the translations of laboratory settings to fruition, to the public, are often special initiatives that do not fit into the mold of research project grants. The Cancer Institute director has bemoaned this from time to time to say we are our own worst enemy and we should all be doing research project grants. On the other hand, I think the real success of the Cancer Institute in the past has been the result of the special authority and special mechanisms that have been impacted negatively by the requirement to fund a specific number of grants. The program project grants are perhaps the best example where you see the translation from the laboratory bench to the bedside. Somehow we've gotten into the tyranny of the accountants where these are counted as one grant."

"That's the kind of information that often slips by in the process," Porter responded. "You are absolutely correct, there is a tyranny of numbers." Porter said there might be a way to encourage NIH to give those grants "a number other than one."

ODAC Oks Carboplatin As First Line Therapy Of Advanced Ovarian Cancer

If the Food & Drug Administration follows the recommendations its Oncologic Drugs Advisory Committee made at its meeting last week:

--Carboplatin (Bristol-Myers Squibb's trade name: Paraplatin) will be approved as first line therapy in combination with other drugs for treatment of stages 3 and 4 ovarian cancer. Carboplatin was approved more than two years ago for advanced ovarian cancer patients who had failed previous chemotherapy.

--A new form of leucovorin, in which the inert d isomer has been removed, leaving the active l isomer, will be approved as rescue for high dose methotrexate in treatment of osteosarcoma. The d,l leucovorin has been used as methotrexate rescue for about 30 years. Lederle Laboratories' trade name for l-leucovorin is Isovorin.

--Pentostatin (Parke-Davis' trade name: Oncopent) will be approved for treatment of hairy cell leukemia refractory to alpha interferon.

--Teniposide, sometimes known as VM-26, will not be approved for treatment of childhood acute lymphocytic leukemia. The indications requested by Bristol-Myers Squibb were for patients who failed induction regimens or who relapsed following remission. VM-26 would have been used in combination with other drugs.

FDA staff appeared to favor the additional indication for carboplatin, l-leucovorin, and pentostatin, which probably means that all three will be approved.

ODAC had rejected carboplatin as first line therapy when it considered the NDA in 1988. Carboplatin was developed as a less toxic analog of cisplatin, and Bristol-Myers claimed that the fact that clinical trials had demonstrated equivalency in response rates would translate into equivalency in survival. However, the survival data were not sufficiently mature for ODAC or FDA to accept, and approval was limited to second line therapy.

With the drug on the market, many physicians prescribed it anyway as first line treatment. Bristol-Myers Oncology Div. distributed publications and other material, mostly unedited reports on trials which further established carboplatin as equal to cisplatin, until the company was forced by FDA to halt those efforts (**The Cancer Letter**, June 28).

FDA reviewer Grant Williams told the committee that "Bristol has shown rather convincingly that overall survival and time to progression are equivalent."

The recommendation to approve Lederle's l-leucovorin was based primarily on preclinical and laboratory studies and very limited clinical data. The committee and FDA staff agreed that Lederle had demonstrated the bioequivalence and bioavailability of l-leucovorin and that it effectively prevented toxicity from high dose methotrexate, which can be fatal if untreated.

However, some committee members wondered why a drug should be approved that is no more than equal to the one it would replace, and possibly more expensive. Lederle responded that l-leucovorin might improve on the modulation of 5-FU over the present d,l leucovorin. The combination of 5-FU and leucovorin is being widely tested for treatment of colorectal cancer, and offers a potentially greater market for leucovorin than does osteosarcoma. Lederle has filed an investigational new drug application for a trial of l-leucovorin and 5-FU.

Lederle also said that l-leucovorin would be only marginally more expensive than the existing agent.

Gregory Burke, acting director of FDA's Div. of Oncologic Drugs, noted that the agency "from the regulatory point of view" must consider only evidence that a new drug is safe and effective. "We can't consider societal or economic factors."

Committee member David Ahmann responded, "We're an advisory committee. We can offer any advice we want. What FDA does with it is up to them." He voted against approval, along with Nancy Kemeny, but it was recommended for approval, in both oral and injection forms, by a 6-2 vote.

In what is now becoming fairly common, pentostatin was recommended for approval on the basis of phase 2 studies. Charles Kowal of Parke-Davis said the drug had achieved a complete response rate of 64 percent and total response of 80 percent in hairy cell leukemia patients who had failed interferon.

Major problem with the data presented by Bristol-Myers Squibb supporting the NDA for VM-26 was that most of the studies had taken place in the 1970s. Committee members argued that its use then could not be considered comparable to present day treatment of childhood ALL. They also suggested the contribution VM-26 makes, in combinations with ara-C and with other agents, is not clear from the studies reported.

The committee voted unanimously against approval for use in combination with ara-C for consolidation after induction of complete response with first relapse while on treatment; five to four against approval for use with ara-C for induction of response in children who are primary induction failures; and seven to two against approval for use in combination with prednisone and vincristine for induction of remission in patients with multiple relapses with or without refractory disease.

'No Greater Honor' Than To Be First Woman NIH Director, Says Healy

"I can think of no greater honor than to be named the first woman director of the National Institutes of Health," said Bernadine Healy after she was formally sworn in late last month.

The June 24 ceremony was attended by President Bush and Barbara Bush, HHS Secretary Louis Sullivan, institute directors, members of Congress and Healy's husband Floyd Loop and children Bartlett and Marie.

In remarks following the ceremony, Healy said she thought of a woman she met recently in a congressman's office, a woman in her thirties with metastatic breast cancer. "She told me with a hopeful smile that she was about to undergo what I knew would be an extremely difficult treatment in a last ditch attempt to stop her cancer. As I left, she took my arm, looked at me intensely, and said, 'Dr. Healy, hurry.'

"Today, I take that young woman's farewell to me as a direct mandate from the American people. NIH and the medical research community must hurry. Human life is at stake, cures are desperately needed, and those cures are achievable--if we have resolve."

Though biomedical science is complex, the basic goals are "to save lives, better health and conquer illness. And, we also can never forget that in this democracy, we work for people like her."

Healy repeated her confirmation hearing statement, which has become bumper-sticker material on the NIH campus: "NIH is a national treasure, and is the premier research enterprise of the world."

She added that NIH "has marshalled a vast force of basic and applied investigators across this country, geared to attack brilliantly any gap in our knowledge of biology and medicine. It has ushered in an era of molecular biology and with it spawned the entire biotechnology industry. It has vastly enriched the quality of life of Americans, and the economic wellbeing of America. But we can, we must, continue to be better. For us there are many wars yet to be won, and each day is our own Operation Bethesda Storm giving hope and seeking victory.... To this end we solemnly pledge to improve the health of this nation through science and discovery. And, to that young mother and her family, and to every man, woman and child who has ever been touched by the anguish of disease--we fervently pledge to each of you--we will hurry."